

A Collection of

**NIDA
NOTES**

**NATIONAL INSTITUTE
ON DRUG ABUSE**

Articles That Address



**DRUG
ABUSE
TREATMENT**

**Department of Health and Human Services
National Institutes of Health
National Institute on Drug Abuse**

Introduction

The National Institute on Drug Abuse (NIDA) supports more than 85 percent of the world's research on drug abuse and addiction. NIDA-funded research enables scientists to apply the most advanced techniques available to the study of every aspect of drug abuse, including:

- genetic and social determinants of vulnerability and response to drugs;
- short- and long-term effects of drugs on the brain, including addiction;
- other health and social impacts of drug abuse, including infectious diseases and economic costs;
- development and testing of medication and behavioral treatments for abuse and addiction; and
- development and evaluation of effective messages to deter young people, in particular, from abusing drugs.

Included in this document are selections of topic-specific articles reprinted from NIDA's research newsletter, *NIDA NOTES*. Six times per year, *NIDA NOTES* reports on important highlights from NIDA-sponsored research, in a format that specialists and lay readers alike can read and put to use. Selections like the current one are intended to remind regular *NIDA NOTES* readers and inform other readers of important research discoveries during the periods they cover.

We hope the information contained here answers your needs and interests. To subscribe to *NIDA NOTES* and for further information on NIDA's drug abuse and addiction research, please visit our Web site at www.drugabuse.gov.

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NIDA's Clinical Trials Network Marks Progress Toward Improved Drug Abuse Treatment

By Robert Mathias, *NIDA NOTES* Staff Writer

More than 300 members of NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN) met in September to celebrate 2 years of progress toward building a nationwide network of researchers and practitioners to conduct clinical trials of promising drug abuse treatments in community settings. The meeting in Crystal City, Virginia, updated participants on the growth of the network, ongoing clinical trials, and upcoming protocols in which they may participate. The meeting also spurred discussion of organizational challenges and other issues that must be addressed to continue to generate clinically useful information from future trials.

"From its inception, the CTN has been marked by an ongoing dialog between researchers and practitioners that has played an integral role in the remarkable growth and evolution of the network," then-NIDA Director Dr. Alan I. Leshner said in a message to meeting participants. "The resulting development of a true working partnership between researchers and practitioners accounts for the extraordinary advances we have made thus far and holds great promise for achieving our mutual goal of making science the foundation for improved drug abuse treatment throughout the Nation."

Among the CTN's accomplishments cited by Dr. Leshner and Dr. Betty Tai, who directs NIDA's CTN Office, are the following:

- The CTN has expanded to 14 regional research and training nodes with 91 affiliated community treatment programs (CTPs) and more than 500 treatment sites.
- Six treatment research protocols with a projected total enrollment of more than 2,600 patients are underway at 52 sites; more than 530 patients have been screened for the trials and 373 have been randomly assigned to receive either an experimental treatment intervention or standard treatment. (See "NIDA Clinical Trials Network Begins First Multisite Tests of New Science-Based Drug Abuse Treatments," V15-6, January 2001.)
- Six additional treatment research protocols are in the final stages of development and will soon be implemented in CTPs.

- A third wave of new research concepts has been approved and is moving toward protocol development. (See "The CTN's First Three Waves of Research Protocols" on next page.)
- Six special interest groups have been formed to focus research plans to address drug abuse treatment issues related to special populations and coexisting conditions, such as HIV/AIDS.

Participants Share Research And Practice Experiences

In a panel presentation, research and practice partners from CTN nodes that pioneered the implementation of the first wave of treatment research protocols discussed issues they confronted in conducting clinical trials in diverse community settings.

CTPs must address staff attitudes before, during, and after initiation of research protocols, several panelists noted. "The commitment to research of everyone in the CTP is critical to successful implementation," noted Dr. Greg Brigham, principal investigator at Maryhaven, Inc., a CTP in Columbus, Ohio, that is part of the Ohio Valley Node. Offering multiple staff training opportunities, keeping key personnel informed about the status of their suggestions and concepts chosen for protocols, and providing feedback on challenges involved in implementing ideas can all enhance staff "buy-in," he said. Frequent conference calls between researchers and clinical staff and providing immediate access to information when it is needed also can help ease research into the clinic.

Conducting research in the CTP placed heavy demands on staff time and clinic resources, such as space, that exceeded their expectations, several CTP representatives cautioned. Because CTN reimbursement does not fully justify the amount of time spent on the protocol, CTP personnel must have other reasons for participating in the CTN, Dr. Brigham said. Dedication to advancing drug abuse treatment, the opportunity to collaborate with the best researchers and practitioners in the field, and recognition by State funding agencies that they are among the leaders in the drug abuse treatment field are some of the bonuses that can encourage CTP participation, he said.

Other panelists discussed additional potential benefits of participating in research. Treatment staff members cited the opportunity to enhance their professional abilities and credentials as substance abuse counselors. CTP administrators noted the potential for generating credible data on effective treatments that could buttress budget negotiations with State funding agencies. For all participants, the realization that their participation could help them to better serve their clients, including the most difficult-to-treat patients, argued for expending the considerable extra effort required. “Conducting one of these protocols requires a tremendous amount of work and sensitivity on the part of both researchers and practitioners to address

practical matters, ethical considerations, and enormous documentation requirements,” said Dr. Leslie Amass of Friends Research Institute, Inc., and the UCLA Integrated Substance Abuse Programs in Los Angeles, which is part of the Pacific Region Node.

“Working with a diverse group of CTPs, ranging from drug-free clinics to hospital-based programs that are carrying out the buprenorphine/naloxone opiate detoxification treatment protocols, has been extremely rewarding for researchers because of the cooperation we are getting. We have more work to do, but we are seeing patients get better and the gap between research and practice is being bridged,” she concluded.

The CTN’s First Three Waves of Research Protocols

The criteria for selecting the first three waves of research protocols developed by NIDA’s National Drug Abuse Treatment Clinical Trials Network (CTN) reflect the growing sophistication of CTN participants as they gain experience in conducting research studies in clinical settings:

- The first wave of protocols is being tested now in the CTN’s community treatment programs (CTPs). These protocols were based on scientific evidence of effectiveness and the ease with which they could be implemented across the network and transferred into practice, said Dr. Betty Tai, director of NIDA’s CTN office. They include pharmacological studies of the effectiveness of buprenorphine/naloxone (BUP/NX) in facilitating opiate withdrawal and studies testing the effectiveness of motivational enhancement therapy and offering prizes as incentives in keeping patients drug free.
- The second wave of protocols now getting underway in the CTPs is designed to complement and build on the first set of protocols. One study will define current CTP practices and staff attitudes to establish a baseline for assessing whether and how innovative practices and treatments are adopted. Two new BUP/NX studies will extend clinical research on that medication by assessing the effect of tapering doses over time and its effectiveness with adolescents who abuse heroin. Other protocols will study infectious diseases and drug abuse and smoking cessation treatment in substance abuse programs.
- The third wave of approved treatment research concepts is now being shaped into protocols for implementation. Unlike earlier research concepts, which were selected primarily by the CTN’s Steering Committee, this third wave of concepts was generated and refined by researchers and practitioners working together in CTN nodes across the network. The concepts continue to broaden the research focus by addressing drug abuse-related treatment issues such as HIV prevention and treatment, and also the treatment needs of special populations, such as substance-abusing pregnant women, women with trauma histories, and adolescents. **NN**

Blood Pressure Medication May Improve Cocaine Treatment Results in Patients With Severe Withdrawal Symptoms

By Robert Mathias, NIDA NOTES Staff Writer

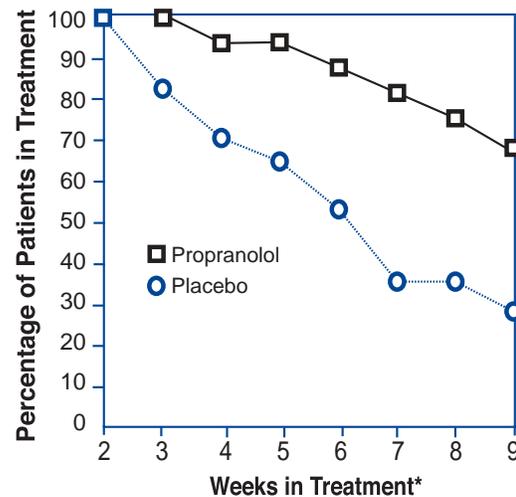
A medication used to treat high blood pressure may be an effective add-on therapy for cocaine-dependent patients who suffer severe withdrawal symptoms when they stop using the drug, a NIDA-funded study indicates. Patients who experienced severe anxiety and other symptoms and were treated with the medication—propranolol—stayed in treatment longer and used less cocaine than a comparable group of patients who were treated with a placebo, the study shows.

Cocaine-dependent patients who experience severe withdrawal symptoms generally use cocaine heavily and are more dependent on the drug than patients who have less severe withdrawal symptoms. “These patients are unable to stop using the drug for significant periods and are more likely to drop out of treatment programs,” says Dr. Kyle Kampman of the University of Pennsylvania School of Medicine in Philadelphia, who conducted the study. “This is not a tiny subgroup. We’ve found that about 40 percent of the cocaine abusers who come into the Day Treatment Program of the Philadelphia Veterans Affairs Hospital have withdrawal severity scores that are high enough to put them at risk for doing poorly in treatment.”

Dr. Kampman and his colleagues theorized that propranolol might lessen the severity of symptoms such as anxiety and craving experienced by newly abstinent cocaine treatment patients. Propranolol belongs to a class of medications called beta-adrenergic blockers that inhibit the effects of adrenaline in the central and peripheral nervous systems, where it works to arouse the body’s “fight or flight” response to dangerous or stressful situations. Beta-adrenergic blockers have been used clinically to treat general anxiety and anxiety associated with alcohol withdrawal. The researchers thought propranolol’s tempering of symptoms such as palpitations and sweating might also reduce cocaine craving associated with such symptoms.

In the study, the researchers used an interviewer-administered questionnaire, the cocaine selective severity assessment (CSSA), to measure cocaine withdrawal symptoms among 108 treatment-seeking cocaine-dependent men and women. The CSSA assesses the intensity of 18 symptoms including anxiety, cocaine craving, depressed mood, appetite changes, sleep disturbances, and altered heart rates that patients may experience when they stop using cocaine. In a previous study, the researchers found that

Effect of Propranolol on Cocaine Treatment Retention In Patients With Severe Withdrawal Symptoms



* Administration of propranolol or placebo began after a 1-week baseline period.

Nearly 69 percent of cocaine treatment patients experiencing severe withdrawal symptoms who received propranolol completed the treatment program, compared to 29 percent of patients with similar symptoms who were treated with a placebo.

patients who had high CSSA scores when they entered treatment were likely to drop out of treatment.

Following a 1-week lead-in period in which all subjects were given a placebo, researchers randomly assigned patients to receive either propranolol or a placebo daily for 8 weeks. All subjects also received cognitive-behavioral counseling twice a week. Urine tests for cocaine were conducted three times a week throughout the trial to assess cocaine use. Treatment retention, cocaine withdrawal symptoms, craving, mood, and anxiety symptoms were evaluated weekly.

When the researchers analyzed results for all study subjects, they found that propranolol-treated subjects had less severe cocaine withdrawal symptoms during the trial, but they did not do significantly better on any other outcome measure than those treated with the placebo. However, when the researchers looked at outcomes in conjunction with the severity of cocaine withdrawal symptoms, they

found that propranolol-treated individuals who had CSSA scores in the upper third of all subjects at baseline were much more likely to complete the treatment program than subjects with similar baseline CSSA scores who were treated with placebo. Among subjects with high CSSA scores, 69 percent of those who received propranolol completed treatment, compared to 29 percent of those treated with a placebo. Propranolol-treated high-CSSA subjects also had significantly lower urine levels of benzoylecognine, a cocaine metabolite, than did placebo-treated subjects, indicating they used less cocaine throughout the trial. There were no significant gender differences in any outcome measures.

Treatment and Research Implications

Although the study's findings are preliminary, they suggest that propranolol may be a useful add-on treatment for the substantial subset of cocaine-dependent patients who have severe withdrawal symptoms. However, treatment outcomes in propranolol-treated subjects were still far from optimal. Additional medication or more intense counseling may be needed to treat such patients effectively, the researchers indicate. "Clinicians can use the CSSA score to predict treatment outcomes and try to match people to appropriate levels of treatment," says Dr. Kampman. "If you put someone with a high score in once- or even twice-a-week individual counseling, they just aren't going to do well. They need more intensive treatment."

The study also has implications for researchers testing cocaine treatment medications, Dr. Kampman says. "Until now, clinical trials haven't separated out those patients who need to be detoxified," he says. "They come in with 'hot' urines [indicative of heavy, current cocaine use], have a lot of withdrawal symptoms, and have trouble getting abstinent. They are so different from people who enter treatment with cocaine-free urines and low withdrawal symptoms, that if you put the two groups together when you test a medication, you are going to miss significant treatment effects. In our studies, we are now dividing patients into two distinct populations based on initial assessment of the severity of their withdrawal symptoms. For patients who have a lot of withdrawal symptoms, we test medications that have the potential to reduce severity of these symptoms to see if it will help them get clean and stay in treatment. For patients who have few withdrawal symptoms and less difficulty achieving initial

abstinence, we select a medication that might work better to prevent relapse."

Additional Medications Research

In addition to propranolol, Dr. Kampman has been testing the potential of other medications to improve treatment outcomes for cocaine-dependent patients with severe withdrawal symptoms. Results of a preliminary trial of amantadine, which may alleviate cocaine's disruption of the brain's dopamine system, were promising. Patients with severe cocaine withdrawal symptoms at the start of treatment used less cocaine during the trial than those who received a placebo.

Following up on these results, Dr. Kampman and his colleagues now are conducting a large, double-blind prospective study of the effectiveness of amantadine and propranolol individually and in combination. The study is targeted specifically at cocaine-dependent patients who score in the upper one-third of patients on the CSSA.

"We know that amantadine slightly increases the release of dopamine, which in turn might reduce the dysphoria—the pervasive unhappiness and restlessness—that also is associated with cocaine withdrawal," says Dr. Maria Majewska of NIDA's Division of Treatment Research and Development. "If amantadine can reduce dysphoria and propranolol can reduce the anxiety and the arousal associated with craving, maybe this will be a winning combination with this population. We are cautiously optimistic as we await the results of the trial."

Sources

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Buprenorphine Taken Three Times per Week Is as Effective as Daily Doses in Treating Heroin Addiction

By Patrick Zickler, NIDA NOTES Staff Writer

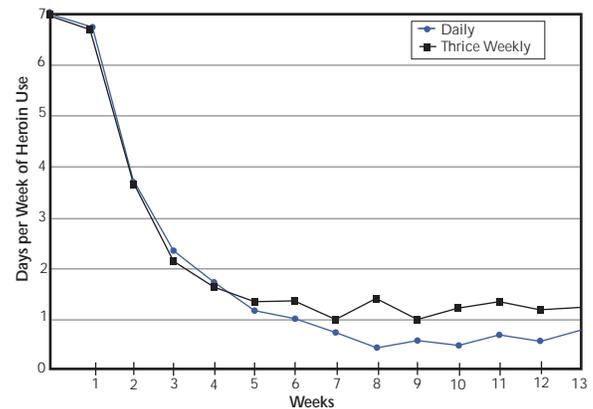
Buprenorphine, a medication developed through NIDA-funded research, has been shown in clinical trials to be an effective treatment for opioid addiction when taken in daily doses. Research at Yale University School of Medicine in New Haven, Connecticut, now suggests that buprenorphine taken three times per week is similarly effective. This finding, says NIDA-supported investigator Dr. Richard Schottenfeld, makes buprenorphine an even more flexible alternative to methadone, a medication that has been used for decades to treat opioid addiction.

Methadone is the most widely used medication for opioid addiction, yet fewer than one in five heroin users now receive methadone treatment for their addiction, Dr. Schottenfeld says. A daily dosing requirement and distressing symptoms of withdrawal that can result from a missed dose cause some heroin users to drop out of or to forgo methadone treatment programs. "Buprenorphine has relatively mild withdrawal symptoms, and a treatment schedule that does not require daily dosing could significantly increase the number of heroin users seeking treatment when buprenorphine becomes available," he says. Buprenorphine is in the final stages of the Food and Drug Administration (FDA) approval process.

Dr. Schottenfeld and his colleagues compared the effectiveness of daily versus thrice-weekly administration of buprenorphine in a 12-week trial involving 92 participants (73 percent white, 75 percent male) who met diagnostic criteria for opioid dependence and FDA criteria for eligibility in methadone maintenance treatment, but who were not currently in treatment. Forty-five participants were assigned to receive daily buprenorphine in an average daily dose of 16 mg per 70 kg of body weight. Forty-seven participants received doses of 34 mg per 70 kg of body weight on Fridays and Sundays, 44 mg per 70 kg of body weight on Tuesdays, and a placebo on other days. All 92 study participants provided urine samples on Mondays, Wednesdays, and Fridays. All samples were analyzed for opioids and cocaine metabolites, and one sample per week from each participant was tested for benzodiazepines.

"There were no significant differences between groups in reduction of opioid use, in retention in the treatment program, or in cocaine use," Dr. Schottenfeld says. "Interviews with the participants suggest that they couldn't reliably tell whether they were receiving the medication daily or three times each week."

Daily or Thrice-Weekly Buprenorphine Doses Yield Similar Declines in Days of Drug Use



Patients in treatment for opioid addiction received either daily or thrice-weekly doses of buprenorphine. Both groups showed reductions in reported days of heroin use during a 13-week treatment program.

Roughly three-quarters of the participants (77 percent of those receiving thrice-weekly and 71 percent of those receiving daily medication) completed the full 12-week program. The proportion of opioid-positive urine samples dropped consistently through the course of treatment (to 57 percent in the daily and 58 percent in the thrice-weekly group), and participants in both groups reported substantial reductions in illicit drug use. The similarity in drug use is evidence that the participants felt no stronger urge to use opioids than those on the daily schedule, Dr. Schottenfeld says. Equally important, he notes, is the fact that both groups were equally likely to stay in treatment, to show up on time for treatment, and to attend regularly scheduled counseling sessions.

In this study, all participants made daily clinic visits even though the thrice-weekly group received medication only every third day. Additional research is needed to determine the effectiveness of thrice-weekly dosing on a schedule that does not require daily contact, Dr. Schottenfeld says. Still, he adds, the finding that thrice-weekly dosing can be as effective as daily dosing in treatment outcome is an important step forward that builds on previous research indicating that some patients would prefer less-than-daily dosing of medication.

“This schedule of treatment could substantially reduce the cost to clinics and the inconvenience to patients. It can also help move use of buprenorphine beyond the traditional narcotic treatment programs and into new treatment settings, such as primary care clinics or physicians’ offices,” Dr. Schottenfeld says.

Source

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NIDA Clinical Trials Network Begins First Multisite Tests of New Science-Based Drug Abuse Treatments

By Robert Mathias, NIDA NOTES Staff Writer

NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN) is up and running. Seven research-based drug abuse treatment protocols are being tested under real-world treatment conditions by the network's 6 pioneering regional research centers in collaboration with more than 35 community treatment programs (CTPs). Approximately 3,000 drug abuse patients are expected to participate in this first wave of clinical trials of promising new pharmacological and behavioral drug abuse treatments.

"The CTN is definitely not business as usual," says Dr. Betty Tai, who directs NIDA's CTN Office. In these studies, researchers and practitioners are breaking new ground by working together to see whether and how treatments that are effective under carefully controlled conditions can be adapted and applied effectively with diverse patient populations in a variety of treatment settings, she says. "We expect that protocols that work under these real-world conditions will quickly become the standard of care for physicians, treatment programs, and their patients," she says.

Goals of the Protocols

The CTN's Steering Committee selected the first treatment concepts for testing using three main criteria—solid scientific evidence of efficacy, ease of implementation, and potential to improve public health, Dr. Tai says. Three broad pharmacological and behavioral treatment research concepts were approved from which CTN protocol development teams produced seven treatment protocols for implementation.

Two pharmacological protocols are studying whether buprenorphine/naloxone (BUP/NX) would be more effective in detoxifying opiate-dependent patients than clonidine, a medication that has been used to detoxify opiate addicts. A related protocol is studying the relative effectiveness of different BUP/NX dosing regimens in detoxifying opiate-dependent treatment patients. BUP/NX is a new medication that is nearing FDA approval for treating opiate addiction. Detoxification, the medically supervised withdrawal from an addicting drug on which a patient is physically dependent, represents the first step in treating opiate addiction. Following detoxification, patients are



Dr. Betty Tai, Clinical Trials Branch, NIDA; Dr. Robert Forman, University of Pennsylvania, Delaware Valley Node; and Paul Nagy, Duke Addictions Program, North Carolina Node, discuss drug abuse treatment at the CTN meeting in October.

treated with a variety of behavioral and pharmacological approaches in many different treatment settings.

The primary objective of the BUP/NX studies is to evaluate the medication's usefulness in detoxifying opiate addicts in both inpatient and outpatient community treatment settings and to determine the most effective dosing regimens. The lead investigator for these studies, Dr. Walter Ling from the University of California, Los Angeles, directs the CTN's Pacific Region Node. A total of 1,080 patients from 14 CTPs in California, Oregon, New York, Pennsylvania, Connecticut, Virginia, and Maryland are expected to participate in these 3 studies.

Two cognitive treatment protocols are adding motivational enhancement therapy (MET) to standard drug abuse treatment. MET is a brief, nonconfrontational treatment in which a clinician seeks to increase patients' commitment to reducing their drug abuse by heightening their awareness of the harmful personal consequences of that use. In one protocol, a therapist delivers MET in three individual therapy sessions during the first 3 weeks of treatment. In the second protocol, called motivational interviewing, therapists use MET techniques only in the intake interview given to patients when they enter treatment.



CTN researchers, treatment providers, and NIDA staff met in Los Angeles in October to discuss new treatment protocols and related issues. From left: NIDA Director Dr. Alan I. Leshner; Dr. Ivan Montoya, Clinical Trials Branch, NIDA; Dr. Dennis McCarty, Oregon Health Sciences University, Northwest Node; Kevin McEneaney, Therapeutic Communities of America, Inc.; Allan Bray, Self Help Addiction Rehabilitation, Inc., Great Lakes Node; and Dr. Kathleen Carroll, Yale University, Southern New England Node.

Both MET protocols are trying to determine if patients who are treated with motivational enhancement techniques stay in treatment longer and reduce their drug use more than patients who receive standard treatment alone. The principal investigator for these studies is Dr. Kathleen Carroll of Yale University in New Haven, Connecticut, who directs the CTN's Southern New England Node. It is anticipated that 1,100 patients from 11 CTPs in California, Connecticut, Virginia, Pennsylvania, Oregon, and New York will participate in these 2 studies.

The last two protocols are assessing the benefit of adding a behavioral treatment called motivational incentive (MI) therapy to standard treatment. One protocol is being tested with patients in methadone clinics and the other in drug-free clinics. MI therapy offers patients tangible rewards for remaining drug free. Patients are given the chance to draw for prizes whenever tests indicate they have not used cocaine, amphetamines, methamphetamine, or alcohol. Abstinent patients can win prizes that range from small items such as candy bars and sodas all the way up to larger items, such as clothing, radios, and TVs. Patients have a better chance of winning smaller prizes than larger ones, but the longer they remain abstinent the more chances they get to win.

The primary objective of the MI protocols is to determine if offering tangible incentives for remaining drug free can keep patients in treatment longer and reduce their drug abuse more than standard treatment alone does. Dr. Maxine Stitzer of The Johns Hopkins University School of Medicine in Baltimore, Maryland, and the CTN's Mid-Atlantic Node is the lead investigator for these studies. A total of 800 patients from 5 methadone treatment programs and 6 drug-free clinics in California, Connecticut, Maryland, New York, and Pennsylvania are expected to participate in these 2 studies.

From Protocol to Practice

"We wanted this first wave of protocols to be easy to implement and transfer into community practice," Dr. Tai says. One of the ways the protocols are accomplishing this is by simply adding the therapy being tested to the standard

treatment normally used in participating CTPs. Patients in the study are assigned randomly to either the enhanced treatment or standard treatment alone. If a study establishes that patients do better with the enhanced treatment than the standard treatment alone, CTPs can simply use the protocol to add the new treatment to standard treatment as needed, Dr. Tai says.

CTN participants modified research-based treatments to enable them to be sustained in practice, says Dr. Tai. For example, the protocols to implement the MI therapy in the CTPs set the total value of rewards that patients can accumulate for staying drug free considerably lower than the total used in research settings. Researchers initially felt that higher rewards might be needed to provide sufficient incentive for drug abuse patients to remain abstinent. However, practitioners were concerned that such awards would prove too costly for their programs. After much negotiation, the CTN's Steering Committee, which is made up of both researchers and CTP representatives, agreed on a middle ground that kept the maximum value of incentives within a range that CTPs felt they could afford. The bottom line was that CTPs would not have been able to support more costly incentives, no matter how well they worked.

"The CTN has made a very good start towards allowing research and clinical practice to impact one another," says Albert L. Hasson, administrative director of the Matrix Institute on Addiction, an outpatient drug-free clinic in the Los Angeles area that is participating in the CTN. "The researchers have ideas about how the research should be done based on what has worked in controlled settings. In turn, the CTPs have ideas about how the research should be adapted and integrated into existing treatment settings to best suit the needs of the programs and the patients they serve.

"Participating in a project of this magnitude has been invaluable for us," says Mr. Hasson, who also serves on the CTN's Steering Committee. "To have input into the direction the research will take has enabled our organization to become part of something that could very well shape the future of drug treatment for years to come." **NN**

Eight New Regional Research Sites Added to Clinical Trials Network

By Robert Mathias, *NIDA NOTES* Staff Writer

NIDA has added eight new regional research centers and their community treatment partners to its National Drug Abuse Treatment Clinical Trials Network (CTN). The expansion more than doubles the size of the nationwide network that NIDA established to conduct multisite trials of promising drug abuse treatments.

The eight new regional centers join the first five centers, which launched the CTN last September, and a sixth center, which was added this February. The 14 regional research and training centers in the newly expanded CTN are linked to more than 85 community treatment pro-

The expansion more than doubles the size of the nationwide network.

grams. Over the next few years, NIDA anticipates adding more research nodes until the CTN reaches a total of 30 to 40 research centers with community treatment affiliates in every area of the country. The 14 current regional research centers and their principal investigators are listed below. **NN**



CTN Approves Second Set of Treatment Research Concepts

Even as the first seven drug abuse treatment research protocols are being implemented in community treatment programs throughout NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN), researchers and practitioners are continuing to propose additional research-based concepts for testing. Recently, the panel of independent experts who make up the CTN's Ad Hoc Oversight Board recommended the approval of the following five new treatment research concepts:

- The effect of buprenorphine/naloxone in treating adolescent heroin addicts;
- Smoking cessation treatment in drug abuse treatment programs;
- An aftercare procedure to reduce relapse following residential drug abuse treatment;
- A survey of obstacles to hepatitis C screening and evaluation in drug abuse treatment programs; and
- An assessment of whether and how the community treatment programs in the CTN are implementing new treatments that are shown to be effective.

More than one protocol is likely to be developed from each of these treatment research concepts. Varying the protocols serves to accommodate the different treatment approaches and settings used by the programs that will implement them. "We envision that eventually the CTN will have 10 to 15 protocols open for enrollment at all times," says Dr. Tai. **NN**

Blending Drug Abuse Research and Practice To Improve Treatment

NIDA Director Dr. Alan I. Leshner

In recent years, NIDA research has produced an array of pharmacological and behavioral interventions that show great promise for improving drug abuse treatment. We know that many of these treatments reduce drug abuse among patients in research settings. We also know that promising new treatments can fail to make the transition from research to practice. By the same token, clinical experiences and observations that could lead to treatment advances do not always get the research attention that they deserve. In this respect, the field of drug abuse is not unique. All fields of medicine have struggled to bridge this disconnect between scientific discovery and assessment and clinical practice.

Now, however, a dramatic change is under way that will bring drug abuse researchers into the real world of the treatment clinic and enable practitioners to participate in treatment research. The instrument of this change is NIDA's

National Drug Abuse Treatment Clinical Trials Network (CTN). The CTN is a cooperative undertaking of NIDA, university drug abuse scientists, and community treatment providers in which researchers and practitioners work together to test research-based treatments in community settings.

In a little more than a year, the CTN has gone from concept to clinical trials, thanks to the efforts of NIDA staff and the researchers and community treatment program (CTP) providers and practitioners from the network's first six regional nodes. Working together to address the many practical obstacles to integrating research and practice, this consortium has established the CTN's organizational structure and operational procedures, selected the first set of promising treatment concepts and developed clinical protocols to test them, trained participating community providers in general and protocol-specific research procedures, and begun implementing the protocols in a variety of community treatment settings. (See "NIDA Clinical



This blending of clinical research and practice will enable the field of drug abuse to realize the full potential of science-based treatments.

Trials Network Begins First Multisite Tests of New Science-Based Drug Abuse Treatments," V16-6, February 2002).

Developing workable protocols for conducting clinical trials in community treatment programs has brought researchers and practitioners together on a regular basis to discuss how to retain the science base of new treatments while modifying them sufficiently to make them practical in the clinic. One of the most important facts this interaction has highlighted is that the road between research and practice is not a one-way street. Valuable

ideas and information about how to improve drug abuse treatment travel in both directions. As a result, we expect that when a CTN study demonstrates that a research-based therapy works in the clinic, the protocol for that treatment will be adopted quickly as a standard of care by CTPs. Likewise, we expect that researchers will take the knowledge gained from working with practitioners back to their laboratories

to inform the design of new treatment studies that meet the real-world needs of the clinic.

This fall, NIDA sponsored a number of new initiatives to build on the progress the drug abuse field is making toward fostering a working partnership of treatment research and practice. These activities include:

- In September, at the CTN's Southern New England Node at Yale University in New Haven, Connecticut, NIDA announced the release of the NIDA Clinical Toolbox, a new package of published resources on the principles and practical delivery of research-based treatment. The Toolbox, which contains the latest scientific information about drug abuse treatment strategies, has been shipped to nearly 12,000 drug abuse treatment programs around the country. (See "NIDA Sends Clinical Toolbox to 12,000 Drug Abuse Treatment Providers.")
- In October, CTN researchers and practitioners from the network's first six regional nodes met in Los

Angeles to welcome their colleagues from new regional nodes. The addition of eight new CTN sites more than doubles the size of the network, extends its reach into additional regions of the country, and expands the scope of its research and communications activities. (See "Eight New Regional Research Sites Added to Clinical Trials Network.")

- In November, the CTN held a regional conference in Los Angeles called "Blending Clinical Practice and Research: Forging Partnerships to Enhance Drug Addiction Treatment Research." At the conference, teams of clinicians and researchers from the CTN presented cutting-edge scientific findings about drug abuse and addiction and real-life perspectives on overcoming obstacles, such as policy and funding constraints, that sometimes inhibit collaboration between researchers and providers. The conference was sponsored by NIDA, the UCLA Drug Abuse Research

Center (which serves as the hub for the Pacific Region Node), the Los Angeles County Alcohol and Drug Program Administration, and The Robert Wood Johnson Foundation.

The CTN's first full year of operation provides compelling evidence that drug abuse treatment researchers and practitioners can work extremely well together toward a common goal-improved drug abuse treatment in the Nation's community treatment programs. By establishing a system for researchers and clinicians to work more closely together in pursuit of this goal, the CTN is not just bridging the gap between research and practice, it is closing it. In time, this blending of clinical research and practice will enable the field of drug abuse to realize the full potential of science-based treatments to reduce the tremendous personal and social costs of drug addiction. **NN**

NIDA Pursues Many Approaches to Reversing Methamphetamine's Neurotoxic Effects

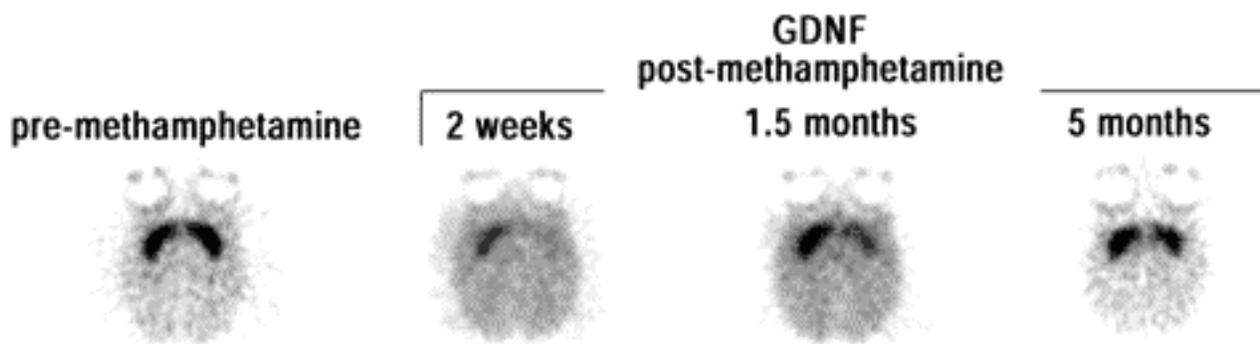
By Robert Mathias, NIDA NOTES Staff Writer

NIDA-supported scientists are pursuing a number of promising approaches to blocking or reversing some of the brain damage wreaked by chronic abuse of methamphetamine. Research has shown that methamphetamine can damage blood vessels and nerve endings in the brain and cause changes in brain chemicals. These effects put chronic methamphetamine abusers at risk for cognitive impairment and early onset of movement disorders associated with aging. (See "Methamphetamine Brain Damage in Mice More Extensive Than Previously Thought.")

In January, NIDA's Division of Treatment Research and Development (DTR&D) convened a "Methamphetamine Addiction Treatment Think Tank." The meeting brought together preclinical and clinical researchers to set up a new program within NIDA's Medications Development Program to develop methamphetamine medications. The program now is selecting and setting up five sites to conduct clinical pharmacology and outpatient studies of medications proposed to treat different aspects of methamphetamine abuse, beginning with methamphetamine addiction. Overdose, neurodegeneration and cognitive impairment, psychoses, and movement disorders will be secondary targets.

"The first priority of the methamphetamine medications development program is to develop medications to treat methamphetamine addiction," says Dr. Ahmed Elkashef of DTR&D, who heads the program. Such medications are aimed at stopping or reducing methamphetamine abuse and not at directly reversing cognitive impairment or other clinical manifestations of methamphetamine's neurotoxic effects when they already have occurred in drug abuse treatment patients, Dr. Elkashef says. However, by reducing drug use, this approach could stop additional neurotoxic damage that might occur with continuing drug use, he says.

In addition to preventing new brain damage, addiction treatment medications may also help treat some of the clinical manifestations of methamphetamine neurotoxicity. "We will assess cognitively impaired patients to see if medications that stop or reduce methamphetamine abuse also improve cognitive functioning," Dr. Elkashef says. Program scientists also plan to test a long list of promising medications that may be able to reverse cognitive impairment caused by methamphetamine abuse, Dr. Elkashef says.



These PET images show brain activity of a chemical messenger called dopamine (shown by dark color) in a monkey that was pretreated with glial-derived neurotrophic factor (GDNF) 1 week before being administered a neurotoxic dose of methamphetamine. Later images showed that the treated monkey had significantly greater recovery of dopamine function than an untreated monkey, at all time points following methamphetamine administration (Brain images by Dr. William P. Melega.)

One of the first compounds the program will test—selegiline—is a medication that has the potential to treat both methamphetamine addiction and its associated cognitive impairment. NIDA has been testing selegiline, an approved treatment for some symptoms of Parkinson's disease, as a cocaine treatment medication. Selegiline's neuroprotective effects counter several possible mechanisms of methamphetamine neurotoxicity, Dr. Elkashef says. "This medication has been shown to reduce cognitive impairments among HIV-positive patients, and we expect it to help treat that aspect of methamphetamine abuse," he says.

Methamphetamine may damage the brain in many ways, including impairment of blood flow, production of harmful free radicals, and killing of brain cells. Thus, the methamphetamine medications development program also is considering using medications that have the potential to improve cognitive function by countering these effects. Potential cognitive enhancers, such as Hydergine, are thought to improve overall brain function by increasing blood flow and brain metabolism. Free radical scavengers, such as vitamin E, boost natural protective chemicals and processes that reduce brain damage caused by free radicals. Hydergine has shown modest success in improving alertness and short-term memory in stroke patients and individuals with Alzheimer's disease. Vitamin E administered with selegiline has slowed progression of Parkinson's disease and reduced severity of abnormal movements in tardive dyskinesia patients.

One possible strategy to address cognitive impairment in methamphetamine-addicted patients would be to add potential cognitive enhancers to drug addiction treatment medications, Dr. Elkashef says. However, the first step with each potential medication will be to assess whether clinical pharmacology interaction studies are needed to make sure it is safe to give it to outpatients who may continue to abuse methamphetamine, he stresses.

Developing Future Treatments

At a much earlier stage of treatment development, NIDA-supported researchers are conducting preclinical studies that could lead to the development of more sophisticated approaches to repairing methamphetamine-induced brain damage. Among the approaches that have shown promising results in animal studies are:

- DADLE ([D-Ala²,D-Leu⁵] enkephalin), a synthetic brain chemical and known tissue-protective agent. DADLE has been shown to block and reverse one type of methamphetamine-induced brain damage in mice;
- Neurotrophic factors, proteins produced by the body that nourish and maintain nerve cells. One of these factors, glial-derived neuro-trophic factor, has been shown to reduce methamphetamine's neurotoxic effects in monkeys;
- Genetic factors and natural anti-oxidants that promote cell survival. Boosting production of these genes and antioxidants in the brains of mice has been shown to prevent or moderate methamphetamine's neurotoxic effects.

Much additional research is needed to design safe and effective formulations of these treatments and ways to get them into the brain before researchers can begin testing in humans. However, these basic studies are increasing understanding of toxic reactions and protective mechanisms in the brain. This understanding should lead to the development of new medications that advance the goals of enabling patients to stop abusing methamphetamine and recover from at least some of the brain damage caused by the drug. **NN**

Gender Differences in Drug Abuse Risks and Treatment

Over the past few years NIDA has made a major research commitment to identifying and understanding differences in the ways that women and men—or girls and boys—are first exposed to drugs, in their risks of abuse and addiction, and in the effectiveness of drug treatment. Understanding these differences, and incorporating that understanding into drug abuse prevention and treatment, can reduce the dangers and improve outcomes. NIDA-supported research has shown that gender differences play a role from the very earliest opportunity to use drugs, that women and men tend to abuse different drugs, that the effects of drugs are different for women and men, and that some approaches to treatment are more successful for women than for men.

Are Women Less Likely Than Men to Abuse Drugs?

Men are more likely than women to have opportunities to use drugs, but men and women given an opportunity to use drugs for the first time are equally likely to do so and to progress from initial use to addiction. However, women and men appear to differ in their vulnerability to some drugs. Both are equally likely to become addicted to or dependent on cocaine, heroin, hallucinogens, tobacco, and inhalants. Women are more likely than men to become addicted to or dependent on sedatives and drugs designed to treat anxiety or sleeplessness, and less likely than men to abuse alcohol and marijuana. There are also differences between men and women who seek treatment for drug abuse. Women in treatment programs are less likely than men to have graduated from high school and to be employed and are more likely than men to have other health problems, to have sought previous drug treatment, to have attempted suicide, and to have suffered sexual abuse or other physical abuse.

Are There Gender Differences In the Biological Effects of Drugs?

Animal research and human studies have revealed that males and females may differ in their biological responses to drugs. In studies of animals given the opportunity to self-administer intravenous doses of cocaine or heroin, females began self-administration sooner than males and administered larger amounts of the drugs. Women may be more sensitive than men to the cardiovascular effects of

cocaine. In human studies, women and men given equal doses of cocaine experienced the same cardiovascular response despite the fact that blood concentrations of cocaine did not rise as high in women as in men. In studies involving long-term cocaine users, women and men showed similar impairment in tests of concentration, memory, and academic achievement following sustained abstinence, even though women in the study had substantially greater exposure to cocaine. Women cocaine users also were less likely than men to exhibit abnormalities of blood flow in the brain's frontal lobes. These findings suggest a sex-related mechanism that may protect women from some of the damage cocaine inflicts on the brain.

Does Gender Play a Role in Nicotine Addiction?

Women and men are equally likely to become addicted to nicotine, yet women typically smoke cigarettes with lower nicotine content than those smoked by men, smoke fewer cigarettes per day, and inhale less deeply than men. Overall, however, women are less successful than men in quitting smoking and have higher relapse rates after they do quit. Treatment involving nicotine replacement therapy—nicotine gum or patch—works better for men than for women.

What Are Women's Risks for HIV/AIDS?

Research suggests that there are sex-related differences in some fundamental aspects of the HIV/AIDS disease process. For example, an HIV-infected woman with half the amount of virus circulating in the bloodstream as an infected man will progress to a diagnosis of AIDS in about the same time. And, according to the Centers for Disease Control and Prevention, among cases that progress to a diagnosis of AIDS, drug abuse accounts for a greater percentage of cases among women than among men. Nearly half (47 percent) of all women diagnosed with AIDS are injecting drug users (IDUs), whereas among men, IDUs account for 32 percent of AIDS cases. An additional 19 percent of women, compared with 2 percent of men, with AIDS report having sex with users who inject drugs. In all, drug abuse is nearly twice as likely to be directly or indirectly associated with AIDS in women (66 percent) as in men (34 percent).

For More Information

NIDA's gender-related research is discussed in Drug Addiction Research and the Health of Women, available on NIDA's home page on the World Wide Web:

www.drugabuse.gov or from the National Clearinghouse for Alcohol and Drug Information (NCADI), P.O. Box 2345, Rockville, MD 20847-2345, (800) 729-6686. **NN**

Treating the Brain In Drug Abuse

NIDA Director Dr. Alan I. Leshner

Remarkable research and technological advances in the past two decades have proved that brain disruption and damage play central roles in the consequences of drug abuse and addiction. Knowing the nature of a problem, of course, opens the way for systematic attempts to fix it. Thus, today, finding ways to restore normal brain function after it has been changed by drugs is a main goal of NIDA research. (See "NIDA Pursues Many Approaches to Reversing Methamphetamine's Neurotoxic Effects.") This goal involves two challenges:

- To reverse the brain changes that underlie addiction, and
- To roll back the loss of cognitive and motor functions that occurs when drugs damage and kill brain cells.

To approach the first challenge, NIDA gives top priority to mapping the sequence of neurobiological changes that takes place during the transition from voluntary to compulsive drug taking. Researchers have already identified some of the changes involved in two of the key phenomena associated with addiction: drug tolerance and drug craving. With respect to drug tolerance—the abuser's need for increasing amounts of drug to achieve the desired effect—we now know that drugs significantly increase the availability of dopamine, a neurotransmitter that activates the brain's pleasure circuits. When cells are exposed to repeated surges of dopamine due to chronic drug abuse, they may eventually become less responsive to dopamine signals. In recent months, researchers presented evidence pointing to a specific change in the dopamine receptor molecule that may be instrumental in this loss of responsiveness.

As for drug craving—the intense hunger that drives addicts to seek drugs despite the strong likelihood of adverse consequences—researchers have shown that it is related to widespread alterations in brain activity, but especially to changes in the nucleus accumbens area of the forebrain. An important type of craving experienced by addicts, called cue-induced craving, occurs in the presence of



Finding ways to restore normal brain function after it has been changed by drugs is a main goal of NIDA research.

people, places, or things that they have previously associated with their drug taking. Brain imaging studies have shown that cue-induced craving is accompanied by heightened activity in the forebrain, the anterior cingulate, and the prefrontal cortex—key brain areas for mood and memory. A next step in understanding craving will be to learn what brain processes tie drug abusers' memories so strongly to the desire to take drugs.

Researchers have also made a solid start toward meeting the second challenge posed by drugs' effects on the brain: the restoration of cognitive and motor capabilities lost because of drug abuse. Studies have identified specific brain changes that are likely causes of the persistent losses that are caused by many drugs of abuse. For example, they have shown that:

- Inhalants can produce a variety of deleterious effects—including reduced vision and hearing, impaired movement, and lowered cognitive ability, sometimes to the point of dementia—by stripping the protective myelin sheath from brain fibers;
- Cocaine causes repeated microscopic strokes in the brain, leading to dead spots in the brain's nerve circuitry;
- Methylenedioxymethamphetamine (MDMA) damages serotonin-producing neurons, which play a direct role in regulating aggression, mood, sexual activity, sleep, and sensitivity to pain;
- As reported on page 1 in this issue, methamphetamine amplifies apoptosis—the normal process by which the brain culls defective cells—to the point where it also eliminates healthy cells.

In extreme cases, drugs can cause such severe destruction that users become severely disabled. For example, some methamphetamine abusers have developed a syndrome marked by uncontrollable tremors similar to those seen in Parkinson's disease. The method of heroin self-administration by inhalation known as "chasing the dragon" has

rendered some young people nearly comatose with large brain lesions.

To counteract the drug-related brain disruptions that produce addiction and cognitive and motor problems, researchers are seeking to mobilize two important brain capacities. First, under the right circumstances, the brain can self-repair some types of damage.

Second, the brain is plastic—that is, when cell losses disrupt the neural circuits that the brain has been using for a specific function, it can learn to use other circuits to perform that function. Plasticity is extremely powerful, as shown by numerous patients' recoveries from extensive cerebral injuries.

Treatments that alleviate some drug-related brain damage are already here. In fact, in recent months, researchers have demonstrated that methadone therapy ameliorates a particular biochemical abnormality in the brains of opiate abusers. The longer patients stayed in therapy, the more this aspect of their brain biochemistry approached normal. NIDA is currently supporting several similar projects that use new brain imaging techniques to evaluate the full impact of current medication and behavioral treatments on brain neurology and biochemistry. Ultimately, such imaging is likely to become an important tool for assessing patients' treatment needs, their progress in treatment, and the effectiveness of treatment approaches.

Interventions will be used first to stop ongoing brain damage and repair damaged brain cells, and then to retrain the brain.

Ultimately, researchers envision a two-stage process for helping restore drug abusers' impaired abilities.

Interventions will be used first to stop ongoing brain damage and repair damaged brain cells, and then to retrain the brain. The rationale for this approach is that repairing the brain first will restore lost mental resources and capacities that patients then can apply in further treatment.

Both behavioral and medication treatments may prove to be effective for both stages of treatment. The first stage may benefit from medications already in use to treat neurological conditions that produce brain abnormalities similar to those associated with abuse of some drugs. For example, deprenyl (used in Parkinson's disease) and acetylcysteine (being tested in Lou Gehrig's disease) have the potential to help people with drug-related neurological damage.

The new knowledge produced by drug abuse research not only brings present goals closer, it also makes possible new and farther-reaching goals. Today we are applying our understanding of brain processes to the development of treatments that directly target the brain mechanisms of addiction and to the alleviation or reversal of drug-related brain disruption. What we learn in that effort will undoubtedly lead to even more powerful insights and strategies for reducing drug abuse and addiction and their health and social consequences. **NN**

Conference Focuses on Linked Issues of Drug Abuse, HIV, and Hepatitis C

By Josephine Thomas, *NIDA NOTES* Contributing Writer

The intricate relationships between the epidemics of drug abuse, HIV/AIDS, and hepatitis C were the focus of discussion at "Drug Use, HIV, and Hepatitis: Bringing It All Together," a conference sponsored jointly by NIDA, the Center for Substance Abuse Treatment (CSAT), and the Centers for Disease Control and Prevention (CDC) held in Baltimore in May.

"The connection between drug abuse and HIV has been recognized for some time," said NIDA Director Dr. Alan I. Leshner. "It's unfortunate that it has taken us this long to take on hepatitis C as a related issue, because the reality is that these three diseases are intertwined." Dr. Leshner emphasized that a logical approach to preventing the spread of HIV and hepatitis C is treatment for drug addiction.

Like HIV, the hepatitis C virus (HCV) is spread through contact with an infected individual's blood and—although this is less common than with HIV—through sexual contact. According to CDC, approximately 4 million Americans have been infected with HCV, of whom 2.7 million are experiencing chronic symptoms. At least 60 percent of the estimated 36,000 individuals infected each year will contract the disease through the use of contaminated injection drug equipment. Eight thousand to 10,000 Americans are expected to die of HCV-related liver disease this year. (See "Facts About Drug Abuse and Hepatitis C," V15-1).

At workshops during the conference, scientists from NIDA and CDC discussed ways to prevent the spread of HCV, as well as ways to assess and treat patients with both HCV and HIV. Attendees participated in skills building workshops that were led by NIDA researchers and other experts and that focused on topics such as the problem of HCV in the prison system; the role of microbicides in prevention; prevention strategies for high-risk populations; the epidemiology of HIV and hepatitis infections among young adults and recently initiated injection drug users; prevention of opportunistic infections; improving adherence to prevention and treatment strategies; integrating treatment into public health settings; methods for conducting patient needs assessments; drug interactions; integrating mental health care into comprehensive treatment planning; and more.



NIDA Director Dr. Alan I. Leshner and CSAT Director Dr. Westley Clark at the conference. (Photo courtesy of Danya International, Inc.)

At a press conference held during the meeting, Dr. Leshner announced the release of NIDA's new Community Drug Alert Bulletin on Hepatitis C and also announced that NIDA is publishing the first science-based guide for HIV outreach, entitled *The NIDA Community-Based Outreach Model: A Manual to Reduce the Risk of HIV and Other Blood-Borne Infections in Drug Users*.

Dr. Leshner noted that NIDA, CSAT, and CDC all are working with the scientific community, substance abuse treatment programs, and the HIV community to increase knowledge of these diseases among people at risk and the general public. "Substance abuse prevention and treatment practitioners are on the front lines of preventing and treating HIV, HCV, and other sexually transmitted diseases (STDs) but need to focus on the whole problem—not just one aspect of it," added Dr. Westley Clark, director of CSAT. This means developing and implementing comprehensive approaches that integrate ways to reduce the risk of contracting and spreading these diseases, he noted.

Dr. Leshner noted that although drug abuse and addiction affect everyone in the United States either directly or indirectly, most people deal with the issue based on their individual ideologies and cultural myths. "Advances in

science have fundamentally revolutionized the way we look at the brain and at drug addiction as a brain disease," he said. "We now know that drug abuse is a preventable behavior but addiction is a disease." Treatment is essential because "drug abuse is a major vector for transmission of other diseases, including HIV, HCV and other types of hepatitis, other STDs, and tuberculosis." The challenge not only will be getting drug-abusing and drug-addicted individuals into treatment, but also will be getting those who have not yet entered treatment to change their behaviors, he said.

"We now have the science base we need to understand how these diseases work alone and together, and this must be the foundation of our work," Dr. Leshner said. "What we have learned through the scientific study of the brain helps explain why most addicts can't just stop taking drugs. But this does not mean that they cannot reduce their risk behaviors for related diseases."

Dr. Henry Francis, director of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA), emphasized to participants that drug abusers tend to be as willing to participate in treatment as anyone else if they have regular contact with a primary care

doctor. "CAMCODA's goal is to expand NIDA's treatment portfolio from a focus on how the disease and infection process works to a focus on why and how people are exposed to risk and what is needed to treat and prevent the disease," he said. Because HCV is a significant problem in the drug-injecting population, treatment provided to individuals who have both HIV and HCV must be carefully planned and monitored. Interferon-the standard treatment for HCV-can cause mood disorders and other symptoms that may encourage drug abuse or interfere with treatment for HIV. Drug use should not be considered a contraindication for treatment of either HIV or HCV, he said.

In panel discussions, experts from CDC's Division of HIV/AIDS Prevention told conference participants that HIV infection rates among injection drug users remain high and that Hispanics and African Americans are disproportionately affected by the disease. Since 1992, death rates among AIDS-infected persons have declined dramatically due to the introduction of highly effective antiretroviral medications. However, the infection rate for hepatitis C in this population has risen as the number of deaths from HIV has declined. **NN**

Drug Abuse Treatment Programs Make Gains in Methadone Treatment and HIV Prevention

By Steven Stocker, *NIDA NOTES* Contributing Writer

Drug abuse treatment programs have substantially improved their methadone treatment practices and increased their HIV prevention efforts since the late 1980s, according to recent NIDA-funded research. These improvements appear to be partly the result of NIDA's efforts to improve drug abuse treatment and HIV/AIDS outreach.

Clinical studies conducted in the late 1980s and early 1990s indicated that methadone treatment is more likely to reduce heroin use if the dose level is at least 60 milligrams per day (mg/day), if patients are given a voice in determining their dose levels, and if no restriction is placed on treatment duration. Subsequent research, however, indicated that the majority of the Nation's methadone treatment facilities were dispensing methadone doses less than 60 mg/day, were not giving patients a voice in dosage decisions, and were encouraging patients to stop taking methadone in 6 months or less.

In response to this situation, NIDA and other Federal agencies took steps to improve methadone treatment. NIDA funded an Institute of Medicine report that recommended changes in heroin addiction treatment practices and their regulation. NIDA also funded the development of a quality assurance program that evaluates methadone treatment facilities in terms of patient outcomes. In addition, the Center for Substance Abuse Treatment (CSAT) developed a set of methadone treatment guidelines and distributed them to State substance abuse agencies and treatment providers around the country.

To determine whether these efforts were in fact improving methadone treatment practices, in 1995 Dr. Thomas D'Aunno of the University of Chicago and his colleagues at the University of Michigan in Ann Arbor collected data from 116 methadone treatment facilities located throughout the country and compared them with data collected on these same facilities in 1988 and 1990. Results showed improvement during the 7-year period, particularly regarding methadone dosage. The average dose was 45 mg/day in 1988 and 46 mg/day in 1990. By 1995,

however, the average dose had increased to 59 mg/day. Also, more programs were allowing patients to participate in dosage decisions, and more programs were waiting at least a year before encouraging patients to stop taking methadone.

The treatment facilities most likely to conduct HIV prevention activities were those that had more patients at high risk of HIV infection, more resources, and lower patient-to-staff ratios.

"Although these results show that methadone treatment facilities have made substantial improvements, we still need to make more progress," says Dr. D'Aunno. "We found an average dose of 59 mg/day in our sample of treatment facilities, but recent research indicates that doses between 80 and 100 mg/day may be the most effective in reducing heroin use." (See "High-Dose Methadone Improves Treatment Outcomes," V14-5, December 1999.)

The study found differences in treatment practices in different areas of the country and for different population groups. Dr. D'Aunno suggests that efforts targeted at particular groups of programs may be a further step to improve treatment.

Dr. Bennett Fletcher of NIDA's Division of Epidemiology, Services, and Prevention Research agrees that efforts to improve methadone treatment practices should continue but adds that misunderstandings some patients have about methadone may also contribute to the problem. For example, he says, some patients attribute adverse effects to methadone that it actually does not cause. "These patients may develop medical or dental problems while taking heroin, but they don't notice them either because of heroin's analgesic effect or because they are distracted by withdrawal symptoms during abstinence," he says. "Once they're in methadone treatment and physiologically stabilized, the medical or dental problems are unmasked. It is easy to blame methadone for these problems, when in fact they were pre-existing." These misunderstandings may cause some patients to request lower methadone doses or to stop methadone prematurely, says Dr. Fletcher.

The Bandwagon Effect

Dr. D'Aunno, along with colleagues at the University of Iowa in Iowa City and the Centers for Disease Control and Prevention in Atlanta, also evaluated treatment facilities' HIV prevention efforts, including HIV testing, counseling, and outreach. For this project, they used data collected from the sample of methadone treatment facilities plus other substance abuse treatment facilities for a total of 618 facilities.

As with the methadone treatment practices, the investigators found that the facilities had made substantial improvements in their HIV prevention efforts over the period from 1988 to 1995. In both 1988 and 1990, only 39 percent of the facilities provided HIV testing and counseling, but by 1995, 61 percent were providing these services. Also, 51 percent of the facilities in 1988 and 65 percent in 1990 were engaging in HIV outreach, but by 1995 this had increased to 75 percent.

The investigators found that the treatment facilities most likely to conduct HIV prevention activities were those that had more patients at high risk of HIV infection, more resources, and lower patient-to-staff ratios. Also, these facilities generally were publicly rather than privately funded and had clinical supervisors who supported HIV prevention practices.

Perhaps the most important factor in promoting HIV prevention practices, however, seemed to be pressure from

people in the drug abuse treatment field. "When the HIV epidemic first started, many treatment facilities were uncertain how to react," says Dr. D'Aunno. "As some facilities began conducting HIV testing, counseling, and outreach, pressure began to mount for other facilities to do the same. This eventually created a bandwagon effect."

NIDA helped get the bandwagon going by supporting research programs in which scientists worked together with practitioners to develop effective HIV/AIDS outreach techniques, according to Dr. D'Aunno. "These programs set a good example for treatment providers," he says. "The providers saw local researchers and other providers working together on HIV prevention, and they decided to follow their lead."

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NIDA Joins NCI, Robert Wood Johnson Foundation To Launch Tobacco Research Centers

By Patrick Zickler, NIDA NOTES Staff Writer

NIDA, the National Cancer Institute (NCI), and The Robert Wood Johnson Foundation (RWJF) have awarded grants to seven academic research institutions to establish Transdisciplinary Tobacco Use Research Centers (TTURCs) devoted to investigating new ways to combat tobacco use and nicotine addiction. The institutions will receive \$70 million from NIDA and NCI for the project. RWJF will provide an additional \$14 million over 5 years to support improved communications and policy development at the TTURCs.

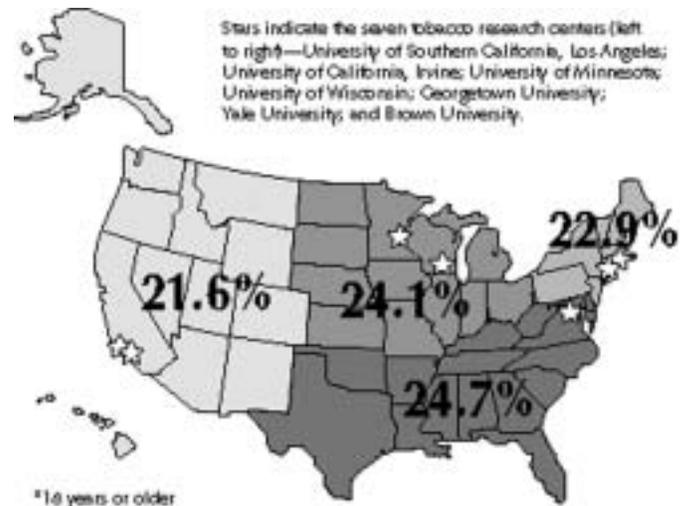
In the past, research grants typically have focused on single components of tobacco use and nicotine addiction, treatment, or prevention, notes Dr. Jaylan Turkkan, chief of NIDA's Behavioral Sciences Research Branch and coordinator of NIDA's TTURC efforts. "The transdisciplinary approach will bring together collaborators who will have the freedom to investigate wider aspects of nicotine addiction, such as factors that influence smoking initiation, and to study the issues at levels ranging from genetics to peer interactions," Dr. Turkkan says.

"The transdisciplinary centers represent an important new approach to research," says NIDA Director Dr. Alan I. Leshner. "Tobacco use and nicotine addiction are incredibly complex subjects, and transdisciplinary investigation can give us the broad perspective we need to understand the etiology of this addiction. This approach will lead to the development of new interventions that will help prevent tobacco use, particularly among teens and younger children."

The TTURC concept evolved from informal conversations among researchers and policymakers at a July 1998 conference—"Addicted to Nicotine"—cosponsored by NIDA, RWJF, NCI, and the Centers for Disease Control and Prevention. Several months later, NCI's Tobacco Research Implementation Group recommended transdisciplinary centers as its highest tobacco use research priority. Within a year, NIDA and NCI jointly issued a Request for Applications from academic centers interested in developing such centers. The first TTURC awards were announced in October 1999. The centers, principal investigators, and research areas are:

- Brown University Center for Behavioral and Preventive Medicine at the Miriam Hospital,

Percentages of Adults* Who Smoke Cigarettes



Although the prevalence of adult cigarette smokers is high, the numbers reflect only one piece of the problem. NIDA's new research centers will seek ways to combat all types of tobacco use among all population segments, adults and children alike. Statistics from Centers for Disease Control and Prevention in Atlanta.

Providence, Rhode Island; Principal Investigator Dr. David Abrams; Research Area Identification of early childhood and lifetime psychiatric factors that determine smoking initiation, dependence, use patterns, cessation, and response to cessation treatment.

- University of California, Irvine; Principal Investigator Dr. Frances Leslie; Research Area Identification of predictors of nicotine addiction in animals and tobacco susceptibility and use in humans;
- University of Southern California, Los Angeles; Principal Investigator Dr. C. Anderson Johnson; Research Area Preventing tobacco use among youth of diverse cultures.
- Georgetown University, Washington, D.C.; Principal Investigator Dr. Caryn Lerman; Research Area Identification of biobehavioral basis of smoking initiation, smoking treatment, and harm from tobacco exposure.

-
- University of Minnesota, Minneapolis; Principal Investigator Dr. Dorothy Hatsukami; Research Area Treating smokers who have been resistant to conventional methods of intervention or who have not been previously targeted.

- University of Wisconsin Medical School, Madison; Principal Investigator Dr. Michael Fiore; Research Area Relapse to tobacco use.
- Yale University, New Haven, Connecticut; Principal Investigator; Dr. Stephanie O'Malley; Research Area Treatment of tobacco addiction. **NI**

Some Cocaine Abusers Fare Better With Cognitive-Behavioral Therapy, Others With 12-Step Programs

By Barbara Shine, NIDA NOTES Contributing Writer

New evidence has been found in support of the hypothesis that a cocaine abuser's personal characteristics affect what kind of treatment will work best to reduce his or her drug use. The evidence surfaced in a recent study in a clinic at the San Francisco Veterans Affairs Medical Center (VAMC), in which Dr. Sharon Hall and her coinvestigators at the University of California, San Francisco (UCSF), compared the efficacy of cognitive-behavioral therapy (CBT) with 12-step facilitation (12SF). The study was supported by NIDA and the U. S. Department of Veterans Affairs.

CBT theory holds that our surroundings strongly influence our thinking and behavior, so CB therapists teach their patients new ways of acting and thinking in response to their environment. In the case of CBT for addiction, patients are urged to avoid situations that lead to drug use and to practice drug refusal skills.

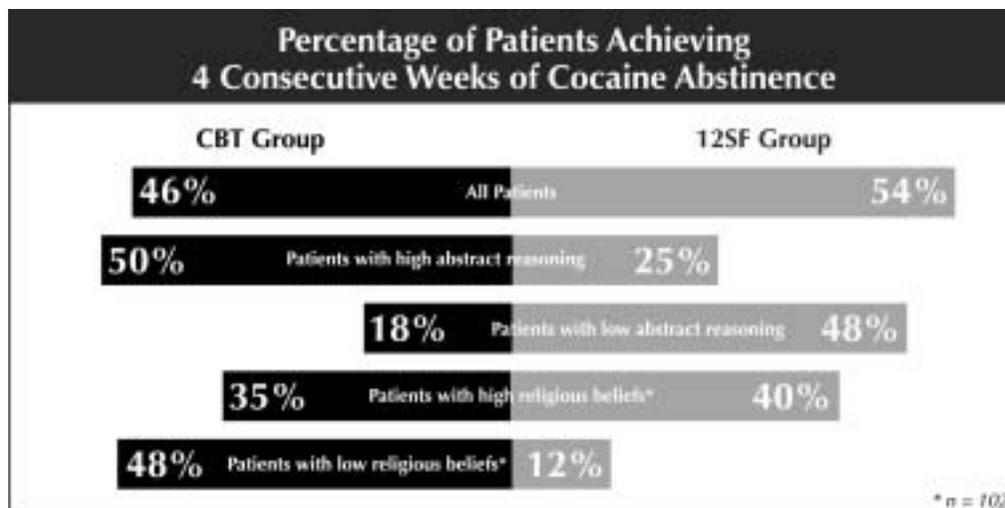
The 12-step recovery method—used in Alcoholics Anonymous and Cocaine Anonymous, for example—involves fellowship and mutual support through regular group meetings as a path toward recovery from addiction. While 12-step programs are not affiliated with any religious group, there is a spiritual component—belief in a "higher power" of some kind that helps members achieve and maintain abstinence.

Dr. Hall and her team recruited 128 crack cocaine smokers from inpatient and outpatient programs at the VAMC. Patients were assigned to either CBT or 12SF. Both groups were expected to attend three group therapy sessions and one individual counseling session each week for 12 weeks.

The CBT approach aimed at helping patients strengthen their commitment to abstinence, deal effectively with urges and risky situations, recognize and change irrational thoughts, manage negative moods, and increase positive moods and social support. Therapists also encouraged participants to attend Rational Recovery, a cognition-based self-help group.

Participants in the 12SF group were introduced to the 12 steps of Cocaine Anonymous and encouraged to work on the first steps of the program. They were urged to attend 12-step meetings in the community in addition to their clinic-based group and individual sessions.

Group therapy was the primary intervention, but individual sessions allowed the therapists to conduct psychosocial histories and develop clinic-mandated treatment plans. In addition, the individual sessions gave participants an opportunity to discuss matters that were not covered adequately in group time.



Patients who were abstinent in the cognitive-behavioral treatment (CBT) tended to have high abstract reasoning scores and low religious motivation scores, while patients who were abstinent in the 12-step facilitation (12SF) program tended to have low abstract reasoning scores and high religious motivation scores.

Content for both CBT and 12SF was organized into manuals. *The Recovery Group Treatment Manual* was based on the work of cognitive theorists A. T. Beck, F. D. Wright, C. F. Newman, and B. S. Liese (Cognitive Therapy of Substance Abuse, New York: Guilford Press, 1993). *The Self-Management Group Treatment Manual* was drawn from J. Nowinski and S. Baker's *Twelve-Step Facilitation Handbook: A Systematic Approach to Early Recovery From Alcoholism and Addiction* (New York: Lexington Books, 1992).

Although participants attended, on average, fewer than half the planned group and individual therapy sessions, the great majority completed their followup assessments, in which urine samples were tested to confirm abstinence from cocaine. Eighty-nine percent of all participants were tested at the final, 26-week followup.

Overall, the CBT patients were more likely than 12SF patients to remain abstinent for 4 consecutive weeks. However, when the researchers added the patients' abstract reasoning skills into the analysis, another pattern emerged.

In the CBT group, patients who scored high on a test of abstract reasoning were more likely to achieve a 4-week abstinence than those with low scores. In the 12SF group, the opposite was found: those who scored low on the abstract reasoning test were more likely to achieve sustained abstinence. In addition, in the 12SF group, but not the CBT group, patients with high scores on a scale measuring religious motivation were significantly more likely

than their peers with low scores to achieve 4 weeks of continuous abstinence.

The researchers caution that this study population was not typical of cocaine abusers nationwide: all were veterans, all were homeless or marginally housed, and men were over-represented. Nevertheless, "These findings show that treatment for cocaine abuse can work and that effective treatment can be provided in a typical clinic setting," says Dr. Hall. "Our study reinforces the importance of getting patients into treatment that corresponds to their personal characteristics."

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For More Information

Copies of the CBT and 12SF therapy manuals in manuscript form are available from Dr. Hall at UCSF. Send e-mail requests to smh@itsa.ucsf.edu. 

Nicotine Medication Also Reduces Craving in Cocaine Addicts

By Patrick Zickler, NIDA NOTES Staff Writer

Craving, the almost irresistible urge to use drugs, is one of the most vexing problems associated with drug addiction. Craving is the result of changes that drugs cause in the brain and may be triggered by physical discomfort associated with abstinence from the drug. Craving also may be triggered by external, environmental factors, such as the sights, sounds, and social situations associated with drug use. In this "cue-induced" craving, the urge to use drugs often is powerful enough to cause a relapse to drug abuse months or even years after a person has stopped using drugs.

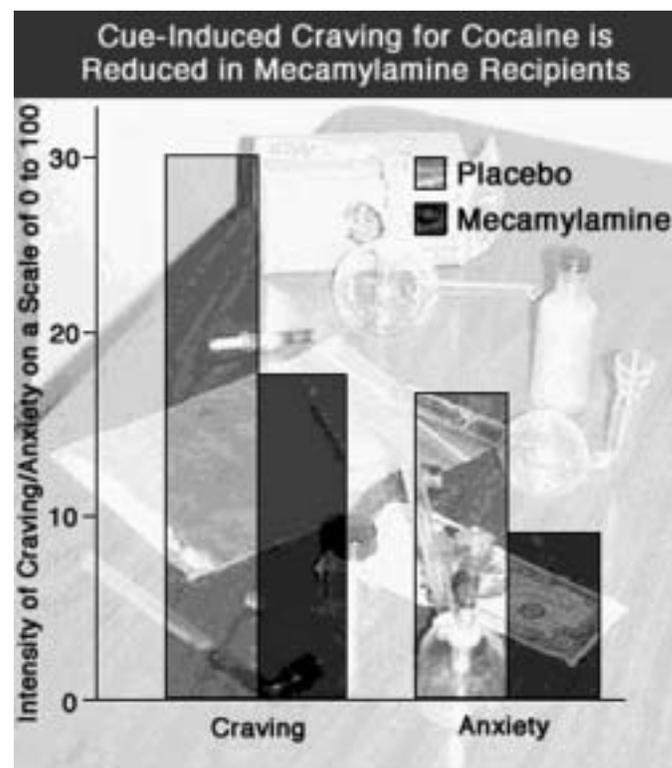
Dr. Malcolm Reid, a NIDA-supported researcher at the New York University School of Medicine and the New York Veterans Affairs Medical Center in New York City, has found that mecamylamine—a medication that blocks the rewarding effects of nicotine—can reduce cue-induced craving in patients addicted to cocaine and may help these patients avoid relapse.

In earlier research, Dr. Reid found that nicotine significantly increased cue-induced craving for cocaine in addicted patients who also smoked tobacco. "This finding suggested that a medication like mecamylamine, which blocks some of nicotine's effects in the brain, might also reduce the cue-induced craving that nicotine causes," Dr. Reid says.

Dr. Reid recruited 23 cocaine-addicted patients, 20 men and 3 women with an average age of 40, from outpatient drug addiction treatment programs. All patients were regular cigarette smokers and had used crack cocaine within the last 3 months. Patients were instructed to abstain from tobacco for at least 1 day and from cocaine for 2 days before participating in the craving test sessions. Abstinence was verified by laboratory tests.

The participants were shown a series of neutral cues as well as cocaine-related cues. During each test session, participants first viewed the neutral cues, including videotaped images of pine cones and seashells, and then handled rocks, pine cones, and seashells and smelled a fragrant spice. Participants then completed a survey that asked them to describe their mood—for example, "anxious," "nervous," or "irritated"—and rate the intensity of their desire to use cocaine and the likelihood that they would use cocaine if it were available. Following exposure to neutral cues, participants were randomly given either

mecamylamine or placebo. Two hours later they were exposed to a series of cocaine-related cues, which included videotaped scenes in which actors simulated purchasing and smoking crack cocaine and scenes of actual crack smoking. The participants then handled drug paraphernalia and a substance that looked like crack cocaine, and smelled a crack pipe that had been treated with an artificial residue with the same aroma as crack cocaine. As before, they rated their mood and desire to use cocaine. The procedure was repeated 2 to 3 days later, with patients who had received mecamylamine during the first session receiving placebo during the second session, and vice versa.



Twenty-three patients were asked to rate the intensity (on a scale ranging from 0 to 100) of their craving for cocaine and their feeling of anxiety after viewing and handling cocaine-related objects like those shown in the background of the graph. Patients who received mecamylamine before exposure to the objects reported significantly less anxiety and craving for the drug.

"Those who received mecamylamine reported significantly less intense cocaine craving—only half as strong on average."

"All the patients reported that they felt an increased craving for cocaine after the cocaine-related cue sessions, but those who received mecamylamine reported less anxiety and significantly less intense cocaine craving—only half as strong on average—than did the patients who received placebo," Dr. Reid says. "In addition, the patients who received the medication reported less intense symptoms of tobacco withdrawal prior to being exposed to cocaine-related cues."

The success of mecamylamine in reducing both cue-induced craving for cocaine and the rewarding effects of nicotine has important implications in treatment. Epidemiologic studies show that smoking is more prevalent among cocaine-addicted persons than in the general population and that cocaine-addicted smokers begin using cocaine at an earlier age and use it more frequently than cocaine-addicted nonsmokers. "In earlier studies we found that nicotine may intensify cue-induced craving for

cocaine, which can make it difficult for cocaine addicts to stop using the drug. We now know that mecamylamine may reduce cue-induced cocaine craving and it does so even when subjects do not have nicotine in their system," Dr. Reid says.

"Previous clinical and preclinical studies have suggested that mecamylamine has therapeutic potential in the treatment of smoking cessation and alcoholism," Dr. Reid notes. "Our current findings indicate it could also play an important role in reducing the risk of relapse for patients in treatment for cocaine addiction." To further investigate this possibility, Dr. Reid is now conducting a clinical trial of mecamylamine treatment of cocaine addiction at the New York Veterans Affairs Medical Center.

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Six Sites Chosen to Launch NIDA Clinical Trials Network

By Robert Mathias, *NIDA NOTES* Staff Writer

NIDA has taken an important step towards improving drug abuse treatment in the United States. The Institute has awarded a total of \$66 million in grants to six university research centers to begin establishing the National Drug Abuse Treatment Clinical Trials Network (CTN). Over the next 5 years, these university centers will collaborate with a range of treatment programs in their respective communities to test, refine, and speed the application of new drug abuse treatments in community treatment settings.

The six university research centers and their community treatment partners are the first of many similar research alliances that NIDA anticipates will be established around the country in coming years. These linked centers and programs will form a nationwide infrastructure for conducting multisite trials of promising drug abuse treatments.

"The Clinical Trials Network will revolutionize drug abuse treatment and drug addiction research," says NIDA Director Dr. Alan I. Leshner. "By establishing a working partnership between researchers and practitioners, the CTN will enable us to take what we learn in the lab and put it into practice rapidly across the country. Equally important, the CTN will enable researchers to take what we learn in the clinic and use it to develop new treatment approaches."

One of NIDA's main goals for the CTN is to build the capacity to test a broad range of behavioral and pharmacological drug abuse treatments in a variety of real-life settings with diverse patient populations. Therefore, the CTN's first six university research centers and their affiliated community treatment programs include a wide array of geographic locales, treatment methods, and patient populations.

The pioneering regional research and training centers range from New England to the Pacific Coast. The centers and their principal investigators are:

- **Southern New England Node**
Yale University
New Haven, Connecticut
Dr. Kathleen Carroll

- **Delaware Valley Node**
University of Pennsylvania
Philadelphia, Pennsylvania
Dr. George Woody
- **Mid-Atlantic Node**
The Johns Hopkins University
Baltimore, Maryland, and
Medical College of Virginia
Richmond, Virginia
Dr. Robert Brooner
- **Pacific Region Node**
University of California, Los Angeles
Los Angeles, California
Dr. Walter Ling
- **Northwest Node**
Oregon Health Sciences University
Portland, Oregon
Dr. Merwyn Greenlick
- **New York Node**
New York University
New York, New York
Dr. John Rotrosen

In the first year of operation, each center will be linked to a minimum of five community treatment programs (CTPs) in its region. These 30 CTPs are located in urban, suburban, and rural settings throughout each region and serve a rich mix of patients including men and women, pregnant women, and adolescents. Patients in these programs span the social and economic spectrum and encompass a variety of racial and ethnic groups. For example, treatment programs in the Pacific Region run the gamut from the Haight-Ashbury Free Clinic in San Francisco to the Betty Ford Center in Rancho Mirage, California.

The CTPs also offer researchers access to outpatient and inpatient treatment settings that provide long-term methadone treatment and shorter term cognitive-behavioral and relapse prevention approaches. These programs treat patients for addiction to a variety of abused drugs including heroin, cocaine, and methamphetamine, as well as a range of conditions that may be related to drug abuse, such as mental disorders and HIV/AIDS.

"The participating community treatment programs are very excited about partnering with researchers to implement new research-based treatment practices," says Dr. Betty Tai, who directs NIDA's CTN Office. "Practitioners at these sites have told us that being part of the CTN also will enable them to scientifically evaluate treatment ideas and modalities that they have been using," she says.

Dr. Tai will represent NIDA on a steering committee that will select promising treatment approaches from among those proposed by all the research alliances for the CTN to investigate in multisite clinical trials. Also serving on that committee will be the principal investigators from

each of the six university centers and a representative from the CTPs in each of the regions.

Initially, the CTN will conduct simple large-scale trials, Dr. Tai says. Once treatment researchers and practitioners have worked together to implement standardized treatments, the CTN will then move on to conduct more complex trials of promising pharmacological and behavioral treatments. "These studies will open the door for practitioners to receive information about new science-based therapies that will help ensure timely dissemination of these therapies," she says. **NN**

Recovery Harder for Addicts Who Start Young

A NIDA-funded study has demonstrated that the relapse rate for heroin addicts increases with time and that the probability of long-run abstinence depends on the age of first drug use. Those who start daily heroin use at a younger age are more likely to relapse than those who start later.

The study, conducted by Dr. Marnik G. Dekimpe of the Catholic University Leuven in Belgium and his colleagues in Belgium and at the University of California, Los Angeles, examined the treatment histories of 846 patients at methadone clinics in central and southern California. The researchers looked at males and females, whites and

Chicanos, most of whom started using heroin between the ages of 17 and 25. Subjects were interviewed over a 4-year period during and after treatment to determine the probability of their relapse to heroin use.

The finding that relapse is connected to time suggests the need for long-term periodic monitoring of a former heroin user's abstinence, Dr. Dekimpe says. The researchers also found drug relapse odds were significantly different across the sociodemographic groups studied, suggesting that prevention resources could be directed to groups at higher risk. No significant differences in relapse probability were associated with either gender or education. **NN**

UCLA Study Looks at Women in Treatment

Women in women-only drug abuse treatment programs were more than twice as likely to complete treatment as women in mixed-gender programs, according to a NIDA-funded study conducted by Dr. Christine E. Grella of the University of California, Los Angeles. The study also found that, on average, pregnant women had used their primary drug for less time than nonpregnant women; and pregnant women in women-only drug abuse treatment programs averaged more days in treatment than did those in mixed-gender programs, 87.4 days vs. 74 days. Overall, pregnant women spent about 15 percent less time in treatment than nonpregnant women.

Dr. Grella's study compared the characteristics of 4,117 women through data reported from 1987 to 1994 by all publicly funded drug abuse treatment programs in Los Angeles County. The statistical analyses of the treatment program data by pregnancy status and gender composition support the premise that women in drug abuse treatment programs have different needs than men in treatment, and a successful program for women often depends on meeting those different needs, Dr. Grella says. **NN**

NIDA Guide Details Research-Based Principles of Drug Addiction Treatment

By Robert Mathias, *NIDA NOTES* Staff Writer

As part of a broad, science-based campaign to help increase the quality and effectiveness of drug abuse treatment throughout the United States, NIDA has issued the first-ever research-based guide to drug abuse treatment. *Principles of Drug Addiction Treatment: A Research-based Guide* will play a central role-along with NIDA's treatment research initiative, nationwide clinical trials network, and manuals that provide up-to-date information on effective addiction treatment-in accelerating the application of research-based treatment components in practice.

Based on more than 25 years of scientific research and clinical practice, the guide lays out 13 overarching principles that characterize effective drug addiction treatment. *Principles* also provides answers to frequently asked questions about treatment, describes types of drug addiction treatment programs, and presents examples of scientifically based components that can be used to enhance treatment programs.

Drug addiction treatment should be comprehensive, include a combination of behavioral therapies and medications, and be tailored to the many needs of addicted patients, according to the guide. In addition, treatment should be accessible, flexible enough to permit modification in response to varying patient needs, and of adequate duration to be effective, the guide states. (See "Thirteen Principles of Effective Drug Addiction Treatment" for more detail and information about how to obtain the guide.)

"Science has revolutionized our fundamental understanding of the nature of drug abuse and addiction and what to do about it," wrote NIDA Director Dr. Alan I. Leshner in an article on drug addiction and its treatment that appeared in the October 14 issue of the *Journal of the American Medical Association*. By articulating the essential characteristics of addiction and effective treatment programs, *Principles* should help both health practitioners and the general public understand and evaluate addiction treatment approaches, Dr. Leshner said.

Principles explains in plain language how drug use changes a person's brain function and behavior over time, leading to addiction and compulsive drug use. Because



drug addiction can interfere with how an individual functions in the family, workplace, and community, drug addiction treatment must include a range of components that can address the unique combination of biological, social, and behavioral aspects of addiction presented by each patient, the guide stresses. A broad selection of such

research-based behavioral and pharmacological treatment approaches is provided and sources of additional details on each approach are listed.

The guide also provides scientifically based explanations to dispel common misconceptions about drug addiction and its treatment. For example, it explains that medical detoxification, which safely manages the physical symptoms of withdrawal from drug use, is only the first stage of addiction treatment and does little by itself to help addicts achieve long-term abstinence. The booklet also counters the common misconception that treatment medications such as methadone and LAAM (levo-alpha-acetylmethadol) are merely addictive substitutes for heroin by describing the marked differences in pharmacological, physiological, and behavioral effects produced by these medications and heroin. These medications stabilize brain and physiological functions disrupted by chronic heroin abuse, reduce the desire for heroin, and make it possible for patients to benefit from behavioral treatments that can help them lead productive lives, the guide explains.

Source

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High-Dose Methadone Improves Treatment Outcomes

By Patrick Zickler, NIDA NOTES Staff Writer

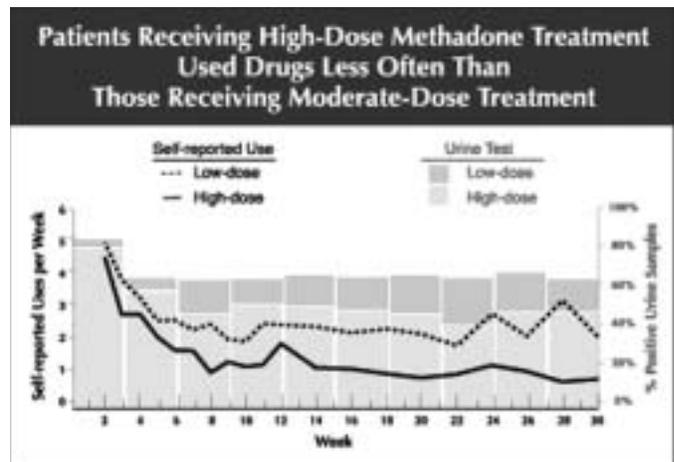
Methadone has been used effectively for more than 30 years as a treatment for heroin addiction. The medication blocks heroin's narcotic effects without creating a drug "high," eliminates withdrawal symptoms, and relieves the craving associated with addiction. Methadone is administered orally in licensed clinics and its effects typically last 24 to 36 hours.

Although methadone has been used for decades, no clinical consensus has been reached about the most effective daily dose. Many clinics do not adjust dosages according to the needs of individual patients. Instead, they administer fixed doses. One clinic might use doses of 25 milligrams (mg) per day for all patients; others may administer daily doses of 60 mg. "Federal regulations require that a clinic receive a special exemption in order to provide patients with doses greater than 100 mg per day, but no contemporary studies have examined the effectiveness of daily doses greater than 80 mg," says Dr. Eric Strain, a NIDA-supported researcher at The Johns Hopkins University Medical Center in Baltimore.

Dr. Strain and his colleagues investigated the effectiveness of high-dose (80 to 100 mg per day) methadone treatment and found this dosage to be more effective in reducing heroin use than treatment with a moderate dose of 40 to 50 mg per day. The study involved 192 patients. Sixty-five percent of participants were male; pregnant women were excluded from the study group.

During the first week of treatment all patients received 30-mg daily methadone doses. Daily doses were increased until, by the 8th week, half the patients were receiving a moderate dose of 40 to 50 mg per day and the other half were receiving a high dose of 80-to-100 mg per day. These doses were maintained through the study's 30th week. Dosages were then decreased by 10 percent each week during the final 10 weeks of the program. Patients were encouraged to enroll in long-term community-based treatment programs following completion of the 40-week study.

Dr. Strain and his colleagues evaluated the effectiveness of treatment through analysis of twice-weekly observed urine testing, weekly patient reports of heroin use, and the length of time patients remained in treatment. "The high-dose group used opiates significantly less during treatment than did the moderate-dose group on average," Dr. Strain



Following a 1-week orientation period, patients receiving high-dose (80-100 mg) methadone treatment had less self-reported heroin use and lower rates of drug-positive urine samples than patients on moderate-dose (40-50 mg) treatment. Urine results are shown as 3-week averages of twice-weekly samples.

says. "Patients in the high-dose group reported using opiates no more than once a week. The moderate-dose group reported using drugs two to three times per week on average." Among patients who completed the 30-week active phase, 33 percent of high-dose patients remained in treatment throughout a 10-week methadone phase-out, compared with 20 percent of moderate-dose patients. There were no gender-related differences in outcome for high- or moderate-dose groups, and no difference was reported between the high- and moderate-dose patients for side effects such as grogginess or constipation.

In an earlier study, the researchers found that moderate-dose treatment of 50 mg per day was more effective than low-dose treatment of 20 mg per day. "The current study provides strong evidence that we can achieve much better outcomes at dose rates much higher than 50 mg per day," Dr. Strain says.

Dosages exceeding the currently regulated ceiling of 100 mg per day may provide the best result for some patients, Dr. Strain says, but he notes that clinical trials would be needed to support changing this regulation. "The most important aspect of our research from a therapeutic and public health perspective is that methadone treatment over

a broad range of doses results in significant clinical improvement for opioid-addicted patients," he says.

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Adding More Counseling Sessions and 12-Step Programs Can Boost Drug Abuse Treatment Effectiveness

By Robert Mathias, *NIDA NOTES* Staff Writer

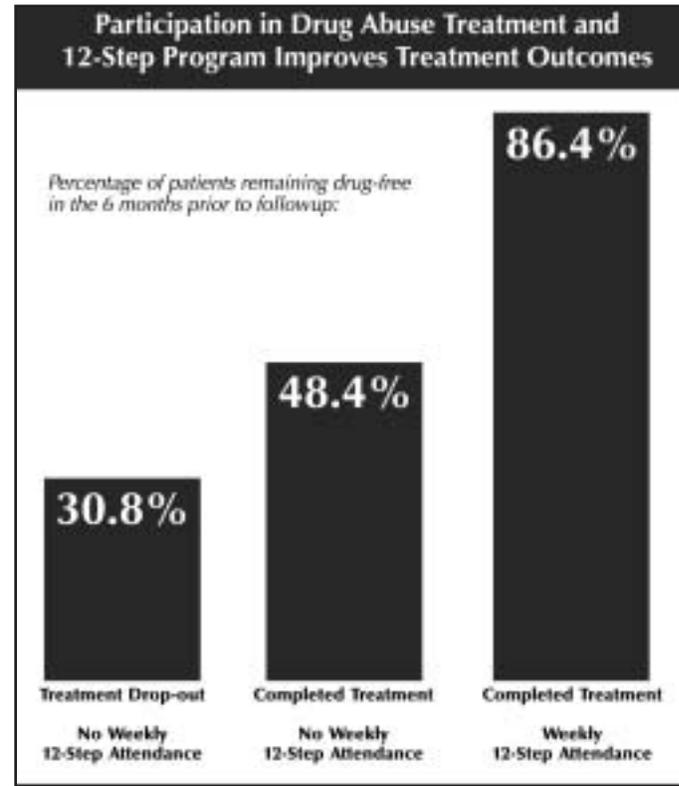
Drug abuse treatment programs can significantly increase the likelihood that patients will stay in treatment and remain abstinent by offering them more group and individual counseling opportunities and encouraging them to participate in complementary 12-step programs, such as Narcotics Anonymous, according to NIDA-supported research.

A series of studies by Dr. Robert Fiorentine of the University of California, Los Angeles (UCLA) and his colleagues from the UCLA Drug Abuse Research Center has been looking at how individual treatment components affect patient outcomes. One study found that patients who attended more group and individual counseling sessions had significantly lower levels of drug use during and after treatment than those who participated less frequently. Even among patients who completed the treatment program, those who participated more frequently in counseling had lower rates of relapse than those who participated less.

Increasing Counseling Opportunities

Dr. Fiorentine then examined whether treatment programs could improve their effectiveness by providing more opportunities for patients to participate in counseling. This study assessed the treatment outcomes of 330 patients in 26 Los Angeles outpatient programs. Seventeen programs had added treatment services and increased counseling opportunities by hiring additional counselors.

This study found that patients in the enhanced programs attended about four more group counseling sessions and one more individual counseling session each month than did patients in comparison programs. Patients in enhanced programs also used drugs 40 percent less than did patients in comparison programs in the 6 months following an initial in-treatment assessment; in the last month, they used drugs 60 percent less. When the researchers examined whether patient characteristics or other treatment services provided by enhanced programs may have affected these results, they found that the frequency of patients' participation in individual and group counseling accounted for virtually all of the differences in post-treatment drug use.



This study suggests that even minimal increases in counseling opportunities may produce impressive gains in treatment outcomes, the researchers note. By hiring only one or two additional counselors, enhanced programs could reduce their counselors' caseloads and offer more group and individual counseling sessions, Dr. Fiorentine says. "It was only a few more sessions per week but, since patient attendance in these sessions often depends on session availability, it made a difference," he says.

Adding 12-Step Programs

Because many patients in Los Angeles area treatment programs attend 12-step programs either on their own or as part of their treatment regimen, Dr. Fiorentine and his colleagues also examined the relationship between participation in such programs and the effectiveness of drug abuse treatment. One study found that patients who attended at least one 12-step meeting per week after

completing drug abuse treatment had much lower levels of drug use than those who participated less frequently or not at all. In this study, the researchers interviewed 262 patients in 26 Los Angeles area drug abuse treatment programs during treatment and 6 and 24 months later. Almost half of these patients had attended a 12-step meeting in the 6 months preceding the last interview.

During this 6-month period, only about 22 percent of weekly 12-step participants had used an illicit drug. By contrast, 44 percent of those who attended 12-step programs less than once a week or not at all during that period had used an illicit drug. Additional analyses indicated that the more favorable outcomes of frequent 12-step participants could not be attributed to differences in motivation or to other posttreatment activities, such as attending other aftercare programs. Weekly 12-step participants did score slightly higher than nonparticipants on a scale of self-reported measures of recovery motivation. However, statistical analyses indicated the differences in motivation accounted for little if any of the more favorable outcomes for frequent 12-step participants. The important difference between the two groups was not recovery motivation but at least weekly 12-step participation, the researchers say.

This study's findings suggest that 12-step programs can serve as a useful and inexpensive aftercare resource that can help many patients to maintain abstinence from drugs and alcohol after they complete drug abuse treatment, say the researchers.

Findings from another study by Dr. Fiorentine indicate that participation in 12-step programs before and during drug abuse treatment also may benefit patients' treatment engagement and recovery. In this study, more than two-thirds of 419 patients who entered outpatient treatment programs in Los Angeles during a 2-month period were attending 12-step meetings in the 3 months before they entered treatment. About 45 percent were attending meetings at least once a week.

Patients who attended 12-step meetings regularly before entering drug abuse treatment stayed in treatment longer and were more likely to complete the treatment program and participate in posttreatment 12-step programs, the study found. Moreover, an assessment conducted 8 months after the initial intake interview showed that patients who attended 12-step meetings at least once a week while they were participating in conventional drug abuse treatment had significantly higher rates of abstinence than patients who participated in only one or the other of those programs.

These findings suggest an "additive effect" on the recovery process from concurrent participation in drug abuse treatment and 12-step programs, Dr. Fiorentine says. "You get a better outcome with both than if you do either alone," he concludes.

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The State of the Art in Drug Addiction Treatment

NIDA Director Dr. Alan I. Leshner

NIDA's recent publication, *Principles of Drug Addiction Treatment: A Research-based Guide*, distills the lessons of 25 years of scientific investigation. Principles is written for health care providers, to stimulate their awareness of the variety of effective approaches to drug treatment. It is also for patients and potential patients and their families, to help them understand the nature of addiction and to tell them about scientifically based treatments and what to expect if they enter treatment. And it serves planners and policymakers as well, enabling them to make informed decisions concerning treatment programs.

In short, this book is for you. That is why NIDA mailed a copy in October to every *NIDA NOTES* reader in the United States. If you have not yet read yours, I urge you to do so. If you did not receive a copy or want additional copies to pass on to friends or colleagues, you can obtain copies from the National Clearinghouse for Alcohol and Drug Information, 1-800-729-6686 (NCADI publication BKD347).

Based on a yearlong review of treatment research, Principles describes where we stand today in our quest for the most effective, replicable treatments for drug abuse. The book contains many important messages, but one is central.

Treatment is effective. Scientifically based drug addiction treatments typically reduce drug abuse by 40 percent to 60 percent. These rates are not ideal, of course, but they are comparable to compliance rates seen with treatments for other chronic diseases such as asthma, hypertension, and diabetes. Moreover, treatment markedly reduces undesirable consequences of drug abuse and addiction—such as unemployment, criminal activity, and HIV/AIDS and other infectious diseases—whether or not patients achieve complete abstinence. Research has shown that every \$1 invested in treatment saves \$4 to \$7 in costs related to drug abuse.



That treatment is effective will not be news to treatment providers or to the tens of thousands of individuals and families who have benefited from treatment. Unfortunately, many members of the public still mistakenly doubt that treatment can help someone overcome addiction, perhaps because—as Principles explains—recovery from addiction can be a long-term process and frequently requires multiple episodes of treatment. To these people, the message of Principles is: We have the tools, let's do the job.

By describing the current state of the art, Principles also clarifies the many challenging research pathways that remain to be traversed on the way to our goal of fully effective treatment for every patient. To cite just a few of the more pressing objectives, we need to:

- Understand the complete behavioral and biological mechanisms of addiction

- Obtain a full picture of the transition from drug use to drug addiction and the stages of recovery in order to fashion optimal treatments for patients at every point along that trajectory;
- Understand better how gender affects vulnerability to drug addiction and the response to treatment in order to more appropriately tailor treatments for men and women;
- Develop additional medications for treating opiate addiction and effective medications for addiction to stimulants such as cocaine and methamphetamine;
- Continue to test the effectiveness of treatments in real-life community-based settings.

NIDA is adjusting its organizational structure and has instituted key procedures to expedite the next stage of our treatment research journey. As I write, the Institute is completing the creation of a new Division of Treatment

Based on a year-long review of treatment research, Principles describes where we stand today in our quest for the most effective, replicable treatments for drug abuse.

Research and Development (DTRD). The new Division will facilitate research on combined medication and behavioral treatments, which appears to be an essential strategy for improving many patients' chances of successful treatment outcomes.

With the support of its Medications Development Division, one of DTRD's predecessors, NIDA has developed cooperative links with the pharmaceutical industry that enable NIDA-supported researchers to obtain proprietary chemical compounds for testing as possible medications for drug abuse. As a first fruit of these partnerships, a new cocaine "vaccine" is currently being tested in a large-scale clinical trial. Based on NIDA-supported basic studies, this new medication appears to reduce the desire to use cocaine by blocking the drug's euphoric effects. NIDA also is exploring ways for new medications to reach more of those in need. The demonstrated effectiveness of buprenorphine and naloxone in treating opiate addiction, for example, suggests that these drugs may be safely dispensed by physicians in controlled settings.

With respect to behavioral therapies, NIDA has established a three-stage process for developing, evaluating, and introducing new approaches into mainstream clinical use. The potential of each proposed new behavioral treatment is first explored in a small pilot study. If the preliminary data are promising, the treatment is tested in a full-scale clinical trial. If the trial demonstrates efficacy, clinicians take the treatment out of the research setting and adapt it

as necessary for mainstream use. This new model establishes the first clear benchmarks for testing, comparing, and implementing behavioral treatments. To date, two new treatments have passed the preliminary stage of testing and moved on to the clinical trials stage.

As regular readers of *NIDA NOTES* are aware, the largest initiative in NIDA's history is focused on treatment. This is the National Drug Abuse Treatment Clinical Trials Network (CTN), in which research centers ally with nearby community treatment programs to set research goals and participate in large-scale multisite clinical trials. NIDA recently announced the establishment of the first five CTN locations. Ultimately, the CTN will provide a nationwide coordinating infrastructure with sufficient patient numbers and diversity to enable scientists to optimize treatment effectiveness by matching treatments with appropriate patient groups.

There is a pattern in scientific research in which knowledge and techniques are slowly, painstakingly developed until they reach a critical mass that makes possible a more rapid and direct approach to problem solving. This first edition of *Principles* reflects the power of this pattern of progress to produce epochal advances in public health and welfare. With well-defined questions and powerful new technologies and research techniques coming on line every year, we do not expect to wait very long before publishing the second edition of *Principles*. **NN**

Combining Drug Counseling Methods Proves Effective in Treating Cocaine Addiction

By Patrick Zickler, NIDA NOTES Staff Writer

NIDA's research into treatments for cocaine abuse has identified a variety of effective treatments ranging from group drug counseling to individualized psychotherapies. In a NIDA-funded clinical trial investigating the efficacy of four types of treatment, patients who received group drug counseling combined with individual drug counseling were more likely to reduce their drug use than were patients who received group drug counseling alone or in combination with psychotherapies that are used to treat addictions.

The NIDA Collaborative Cocaine Treatment Study involved 487 patients with relatively low levels of psychiatric severity whose principal diagnosis was cocaine dependence as defined by the Diagnostic and Statistical Manual of Mental Disorders. The drug counseling therapies evaluated in the multisite study are specifically designed to treat drug use; the psychotherapies—supportive-expressive therapy and cognitive therapy—are less focused on drug use.

The study involved patients recruited at five sites—the University of Pennsylvania in Philadelphia; the Western Psychiatric Institute and Clinic at the University of Pittsburgh; Massachusetts General Hospital in Boston; McLean Hospital in Belmont, Massachusetts; and Brookside Hospital in Nashua, New Hampshire. Each research center provided four treatments: group drug counseling alone, group drug counseling combined with individual drug counseling, group drug counseling combined with cognitive therapy, or group drug counseling combined with supportive-expressive therapy. Each of the 487 patients was randomly assigned to one of the therapies. Treatment results were evaluated through patient self-reporting, weekly observed urine testing, and the Addiction Severity Index—an interview-based assessment used to measure treatment outcome.

During each of the 6 months of treatment, and at 3 months and 6 months after treatment ended, patients who received combined individual and group drug counseling used less cocaine and drugs overall than did patients who

received other forms of treatment. A higher percentage of combined drug counseling patients were able to achieve abstinences of 1, 2, and 3 months than were patients in the other study groups. During the 6 months after treatment ended, 38 percent of

patients who completed combined counseling treatment maintained drug-free periods of 3 consecutive months compared with 27 percent of patients treated with group counseling alone, 23 percent of patients treated with cognitive therapy plus group counseling, and 18 percent of

patients receiving supportive-expressive therapy plus group counseling. In addition, patients who received combined drug counseling showed more improvement in Addiction Severity Index ratings than did patients receiving other treatments. "These results underline the valuable role of well-designed drug counseling in treating drug abuse. More specifically, this study demonstrates the effectiveness that combined counseling therapies can have in treating cocaine addiction," notes Dr. Jack Blaine of NIDA's Division of Treatment Research and Development.

"The success of combined drug counseling treatment compared with the psychotherapies may be due to the fact that drug counseling delivers a message that is simple and strong—stay away from the situations where you use drugs and the people you use drugs with. The counselors at all sites involved in our study were able to deliver that message effectively," says Dr. Paul Crits-Christoph of the University of Pennsylvania, who coordinated the multicenter study.

Criteria for Success

"The success of combined drug counseling compared with other treatments is the result of the nature, intensity, and quality of counseling," Dr. Crits-Christoph says. "We paid a great deal of attention to selecting and training counselors, all of whom had extensive previous experience treating patients with substance abuse disorders." The counselors and psychotherapists received more than a year

Patients who received combined individual and group drug counseling used less cocaine than did patients who received other forms of treatment.

of training in standardized therapy using published manuals, and were evaluated during training and certified prior to participation in the collaborative treatment study.

Group drug counseling, given to all study participants, consisted of weekly sessions for the full 6 months of the study and individual meetings with the group counselor once per month during a 3-month "booster" phase following the 6 months of active treatment. Patients in individual drug counseling and psychotherapy treatments participated in twice-weekly sessions during the first 3 months, weekly sessions during the second 3 months, and monthly meetings during the booster phase.

Group drug counseling treatment involved an initial 3-month phase during which patients were educated about the concepts in recovery from addiction, and a second 3-month phase that involved open group discussions focusing on patients helping each other solve problems encountered in recovery. Individual drug counseling focused on helping patients achieve and maintain abstinence through behavioral changes such as avoiding situations that trigger drug use. Group drug counseling and individual drug counseling encouraged patient involvement in self-help and support groups such as Cocaine Anonymous outside of scheduled treatment sessions.

Cognitive therapy involved identifying the underlying beliefs related to a patient's drug use. Therapists worked with patients to evaluate the advantages and disadvantages of their beliefs. They also employed role-playing, behavioral

experiments, and scheduling and monitoring activities. Supportive-expressive therapy involved identifying interpersonal conflicts that relate to a patient's drug use. Therapists helped patients interpret the role that these conflicts play in drug use and problems encountered in stopping drug use.

Because treatment and training were based on published manuals, it may be possible for other treatment programs to achieve similar results, Dr. Crits-Christoph notes. "If other programs can apply these tools with the intensity that characterized this study, their outcomes should be similarly successful."

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Thirteen Principles of Effective Drug Addiction Treatment

More than two decades of scientific research have yielded a set of fundamental principles that characterize effective drug abuse treatment. These 13 principles, which are detailed in NIDA's new research-based guide, *Principles of Drug Addiction Treatment: A Research-based Guide*, are:

1. No single treatment is appropriate for all individuals. Matching treatment settings, interventions, and services to each patient's problems and needs is critical.
2. Treatment needs to be readily available. Treatment applicants can be lost if treatment is not immediately available or readily accessible.
3. Effective treatment attends to multiple needs of the individual, not just his or her drug use. Treatment must address the individual's drug use and associated medical, psychological, social, vocational, and legal problems.
4. Treatment needs to be flexible and to provide ongoing assessments of patient needs, which may change during the course of treatment.
5. Remaining in treatment for an adequate period of time is critical for treatment effectiveness. The time depends on an individual's needs. For most patients, the threshold of significant improvement is reached at about 3 months in treatment. Additional treatment can produce further progress. Programs should include strategies to prevent patients from leaving treatment prematurely.
6. Individual and/or group counseling and other behavioral therapies are critical components of effective treatment for addiction. In therapy, patients address motivation, build skills to resist drug use, replace drug-using activities with constructive and rewarding nondrug-using activities, and improve problem-solving abilities. Behavioral therapy also facilitates interpersonal relationships.
7. Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies. Methadone and levo-alpha-acetylmethadol (LAAM) help persons addicted to opiates stabilize their lives and reduce their drug use. Naltrexone is effective for some opiate addicts and some patients with co-occurring alcohol dependence. Nicotine patches or gum, or an oral medication, such as bupropion, can help persons addicted to nicotine.
8. Addicted or drug-abusing individuals with coexisting mental disorders should have both disorders treated in an integrated way. Because these disorders often occur in the same individual, patients presenting for one condition should be assessed and treated for the other.
9. Medical detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug use. Medical detoxification manages the acute physical symptoms of withdrawal. For some individuals it is a precursor to effective drug addiction treatment.
10. Treatment does not need to be voluntary to be effective. Sanctions or enticements in the family, employment setting, or criminal justice system can significantly increase treatment entry, retention, and success.
11. Possible drug use during treatment must be monitored continuously. Monitoring a patient's drug and alcohol use during treatment, such as through urinalysis, can help the patient withstand urges to use drugs. Such monitoring also can provide early evidence of drug use so that treatment can be adjusted.
12. Treatment programs should provide assessment for HIV/AIDS, hepatitis B and C, tuberculosis and other infectious diseases, and counseling to help patients modify or change behaviors that place them or others at risk of infection. Counseling can help patients avoid high-risk behavior and help people who are already infected manage their illness.
13. Recovery from drug addiction can be a long-term process and frequently requires multiple episodes of treatment. As with other chronic illnesses, relapses to drug use can occur during or after successful treatment episodes. Participation in self-help support programs during and following treatment often helps maintain abstinence.

Principles of Drug Addiction Treatment: A Research-based Guide (NCADI publication BKD347) has been mailed to NIDA NOTES subscribers in the U.S. Copies of the booklet can be obtained from the National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD 20847, 1-800-729-6686. **NN**

Medications Reduce Incidence of Substance Abuse Among ADHD Patients

By Steven Stocker, *NIDA NOTES* Contributing Writer

Attention-deficit/hyperactivity disorder (ADHD) causes difficulties in paying attention, keeping still, and suppressing impulsive behaviors. It can lead to problems in school and on the job and create tensions with family members and other people. In addition, research has shown that children with ADHD have an elevated risk of becoming abusers of drugs and alcohol. Studies that have tracked children to adulthood have found higher rates of transition to abuse among those with ADHD compared to those without the disorder. Conversely, studies with adult substance abusers, particularly cocaine abusers, have found that when they were children a high percentage had ADHD that was undiagnosed and therefore untreated.

NIDA-supported researchers have been trying to learn why ADHD increases the risk of drug and alcohol abuse. Two possible explanations have been suggested. First, the disorder itself may be responsible. Alternatively, the medications used to treat the disorder may be to blame.

ADHD is usually treated with behavioral therapy and prescription stimulants, especially Ritalin® (methylphenidate), Dexedrine®, or Adderall®. Such therapy frequently reduces symptoms, but some clinicians have feared that giving prescription stimulants to children may get them in the habit of taking stimulants, and, as a result, they may be more likely to take illicit stimulants, such as cocaine and methamphetamine. Another possibility is that the use of prescription stimulants for treating ADHD may sensitize the brain to the rewarding properties of stimulants, and, as a result, patients who use illicit stimulants may be more likely to become addicted to them.

Some children treated for ADHD with stimulant medications experience adverse effects, such as tics or loss of appetite. These children may be treated instead with tricyclic antidepressants (TCAs), a class of medications that includes imipramine, desipramine, and nortriptyline. Just as with mild stimulants, some clinicians are concerned that giving these mood-altering medications to children may get them in the habit of taking drugs to feel better and so they may be more at risk of using illicit drugs.

If ADHD treatment medications increase the risk of drug abuse, then using them might do more harm than good over the course of the child's lifetime. However, two new NIDA-supported studies suggest that treatment medications may be part of the solution to drug abuse in ADHD, rather than the problem.

One study found that children who were medicated for their ADHD were less likely to become substance abusers during 4 years of followup than were children with ADHD who were not medicated. The other study found that administering an ADHD medication to adult cocaine abusers with the disorder reduced their cocaine use.

Boys Treated for ADHD Abuse Drugs Less Than Untreated Boys

Researchers at Massachusetts General Hospital and the Harvard Medical School, both in Boston, compared the incidence of substance abuse and dependence in 56 boys with ADHD who were being treated with either stimulants or TCAs at the beginning of the study, 19 boys with ADHD who were not receiving any medications, and 137



Children with ADHD often have trouble concentrating and keeping still, which can lead to problems in school.

boys without ADHD. All boys were Caucasian and were followed for 4 years and then evaluated for abuse of or dependence on marijuana, alcohol, hallucinogens, stimulants, or cocaine. At the time of evaluation, the boys were at least 15 years old.

Treating ADHD with medications appeared to reduce the tendency to abuse drugs and alcohol. While 75 percent of the unmedicated ADHD boys had started abusing these substances in the previous 4 years, this was true of only 25 percent of the medicated ADHD boys and 18 percent of the boys without ADHD. The researchers calculated that treating ADHD with medications reduced the risk of substance abuse or dependence by 84 percent.

Dr. Joseph Biederman, the principal investigator of the study, calls this very important information for the field of pediatrics. "These are the first data to refute the argument that ADHD medications increase the risk that children will become addicts," he says. "There have been studies consistent with these findings for many years, but now we have solid statistical evidence that these medications decrease, rather than increase, vulnerability to addiction, at least in adolescent Caucasian boys."

Why treatment with medications should reduce the incidence of substance use disorders in boys with ADHD is not known, says Dr. Biederman, just as what causes ADHD and how medications reduce ADHD symptoms are also unknown. "I can only speculate that by reducing ADHD symptoms, the medications allow the children to interact better with their families and friends and to perform better in school," he says. "As a result, they are less likely to be ridiculed and rejected by other children and to fail in school. Because of this, they are less likely to be depressed and to take drugs in an attempt to treat their depression." He says that another reason may be that the medications reduce the tendency of ADHD children to be impulsive, which often leads them to engage in risky activities, such as taking drugs.

Other researchers have reported that some adult cocaine abusers with childhood histories of ADHD state that when they first started using cocaine, the drug initially improved their ADHD symptoms. Their concentration improved, they were less impulsive, and they felt calmer. This would suggest that young people with ADHD who abuse cocaine and other stimulants may be doing so to self-medicate their ADHD symptoms rather than to treat depression resulting from rejection and failure.

"In some cases, young people with ADHD are not properly diagnosed and treated, and, as a result, they have terrible problems," says Dr. Arthur Horton of NIDA's Division of Treatment Research and Development (DTRD). "Their lives are not going well, so they try different things to make themselves feel better. They don't

know that Ritalin® will alleviate their symptoms. If they happen to try cocaine, they might find that it initially makes them more focused and able to deal with life, so they keep taking it, and that's how they get hooked."

DTRD Director Dr. Frank Vocci points out that more research needs to be done before definite conclusions can be drawn about the relationship between ADHD therapy and substance abuse. "As it stands, this study clearly supports the idea that medications protect individuals with ADHD from becoming substance abusers during childhood and adolescence," he says. "However, whether or not they become substance abusers when they reach adulthood is still an open question."

Dr. Biederman says that his group is continuing to collect data on his sample as they age. Another followup study is currently under way on the young men, who are now between 16 and 27 years old. This study should help answer the question of whether ADHD medication therapy can protect against substance abuse in late adolescence and early adulthood. The researchers are also following a group of girls with ADHD and a comparison group of girls without ADHD. A key question to be answered will be whether gender differences exist in the effects of stimulants, including the effects on substance abuse.

Treatment That Includes Methylphenidate Helps Adult Cocaine Abusers With ADHD

In addition to helping protect children with ADHD from becoming substance abusers, methylphenidate may also help adult cocaine abusers with ADHD reduce their drug use. In a pilot study, Dr. Frances Levin and researchers at Columbia University in New York City gave methylphenidate for up to 12 weeks to 12 adult cocaine abusers with ADHD. Patients also received individual weekly relapse prevention therapy, which involved identifying situations in which they were likely to return to cocaine use and developing strategies to avoid cocaine use in these situations. Of the 12 patients who entered the study, 7 could be reached for a 3-month assessment. Patients reported a reduction in ADHD symptoms, cocaine use, and craving; urine tests confirmed that their cocaine use had in fact decreased significantly.

At present, Dr. Levin cannot say whether methylphenidate, the behavioral therapy, or a combination of both was responsible for the positive results. To answer this question and to determine whether these preliminary results can be reproduced among other cocaine abusers with ADHD, she is conducting a large clinical trial in which neither the patients nor their therapists know whether the patients are receiving methylphenidate or placebo.

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New NIDA Clinic Tests Therapies to Help Teens Quit Smoking

By Steven Stocker, *NIDA NOTES* Contributing Writer

NIDA's Intramural Research Program (IRP) recently opened a new Teen Tobacco Addiction Treatment Research Clinic at the Bayview Medical Center in Baltimore. At the clinic, researchers will evaluate promising therapies for adolescent nicotine addiction.

One of the clinic's first research projects will be a pilot study of smoking cessation treatments for 13- to 17-year-old cigarette smokers. "More than one-third of 17-year-olds who smoke say they are interested in some form of treatment to help them quit," says IRP's Dr. Eric Moolchan, director of the new clinic and leader of the smoking cessation study.

The research project will test the combination of nicotine replacement therapy (NRT) and group counseling for treating nicotine addiction in adolescents. NRT helps smokers learn to abstain from smoking by replacing the nicotine that they previously obtained from cigarettes, thereby preventing withdrawal symptoms and craving for nicotine. NRT forms currently available include the nicotine patch and gum.

Dr. Moolchan says that many health care providers are reluctant to prescribe nicotine patches or gum for adolescents because of a lack of studies showing that these products are safe and effective in this age group. The IRP pilot study will help determine whether adolescents can use the nicotine patch and gum safely, whether they can tolerate the same nicotine doses in the patch and gum as adults, and whether they will follow the instructions on how to use these products. Later studies will focus more on the effectiveness of the patch and gum in helping adolescents quit smoking.

"It's important that we develop effective treatments for young people to try to get them to quit smoking as early as possible," says IRP Director Dr. Barry Hoffer. "Research shows that 90 percent of people who die



Cutting the ribbon to dedicate NIDA's new Teen Tobacco Addiction Treatment Research Clinic (TTATRC) in Baltimore are, from left, Dr. Jean Lud Cadet, clinical director, NIDA's Intramural Research Program (IRP); NIDA Director Dr. Alan I. Leshner; Dr. Barry Hoffer, director of NIDA's IRP; Dr. Eric Moolchan, director of TTATRC; and Dr. Monique Ernst, IRP researcher.

"More than one-third of 17-year-olds who smoke say they are interested in some form of treatment to help them quit."

prematurely of a cigarette-related disease started smoking when they were adolescents. If we can help adolescents quit smoking, we should be able to prevent many of these premature deaths."

The IRP study will have 3 groups, each with 18 adolescents. The first group will receive active patches containing nicotine and placebo gum without nicotine, the second group will receive placebo patches and active gum, and the third group will receive placebo patches and placebo gum. Participants will not be told whether the products they receive are active or placebo.

All three groups will also participate in group counseling sessions because studies with adult smokers have indicated that smoking cessation programs that combine behavioral therapy with medications produce the highest abstinence rates. In the counseling sessions, a mental health professional and Dr. Moolchan, who is a pediatrician, will discuss various topics involving smoking and health and will teach the adolescents how to modify their behavior to deal with situations that might cause them to smoke.

Even though smoking is the primary focus of the sessions, other topics—such as peer relations, school, and dating—will be discussed. "Addressing these other issues is important

because adolescent smokers often think that smoking helps them in their social relations," says Dr. Moolchan. "Furthermore, problems concerning social relations can negatively affect mood, and smokers often regulate their mood with nicotine."

The IRP project also will examine other aspects of adolescent smoking. One study will analyze how adolescents smoke cigarettes—for example, how deeply they inhale or how many puffs they take per cigarette. IRP researchers will also study whether nicotine withdrawal causes adolescents to experience problems with concentration and

short-term memory and whether nicotine-replacement treatments can reverse these deficits. Another project will measure chemical evidence of cigarette consumption in saliva to determine whether adolescents metabolize the components of cigarette smoke in the same way that adults do.

The researchers will recruit adolescents from the Baltimore area through referrals from healthcare providers, schools, churches, and youth centers. Dr. Moolchan hopes that this study will establish contacts in the community that can be used to recruit adolescents for future studies. **NN**

Drug Abuse and Mental Disorders: Comorbidity Is Reality

NIDA Director Dr. Alan I. Leshner

A quarter century of basic and clinical research has provided us with a substantial number of scientifically developed and tested pharmacological and behavioral techniques for treating drug abuse and addiction. A main thrust of NIDA's current research is to discover which combinations of treatments and services work best for individual patients with particular constellations of problems. The goal is to customize treatment for every patient, including those with coexisting problems such as multiple drug abuse, drug abuse-related infectious diseases, histories of sexual abuse, or homelessness.

Drug abusers who have concurrent, or comorbid, mental health problems are at the top of the list of those who will benefit from this research, for two reasons. First, they are numerous. Recent epidemiologic studies have shown that between 30 percent and 60 percent of drug abusers have concurrent mental health diagnoses including personality disorders, major depression, schizophrenia, and bipolar disorder. Second, drug abusers with mental illness comorbidity are more likely to engage in behaviors that increase risk for HIV/AIDS. For example, two studies of injecting drug abusers have found that anti-social personality disorder (APD) is associated with a higher frequency of needle sharing.

In order to direct treatment and services research to where it is most needed, NIDA supports epidemiologic studies of mental health comorbidities. The results to date suggest that the most common are personality disorders including APD and borderline personality disorder; anxiety disorders including post-traumatic stress disorder (PTSD); and depression. Some evidence suggests that men who use drugs are more likely to have APD, while women and minorities are more likely to have depression or PTSD. While people with schizophrenia do not constitute a large portion of the drug-abusing population, an extraordinarily high percentage of people with this disease abuse drugs.



Recent epidemiologic studies have shown that between 30 percent and 60 percent of drug abusers have concurrent mental health diagnoses including personality disorders, major depression, schizophrenia, and bipolar disorder.

A concurrent mental disorder can complicate drug abuse treatment in a multitude of ways. For example, research suggests that clinically depressed individuals have an exceptionally hard time resisting environmental cues to relapse—that is, urges to resume drug taking that commonly occur when abstinent addicts encounter people, places, or things associated with their previous drug use. In some cases, treatment for mental disorders must be adjusted because of concurrent drug abuse. For example, opiate users with

anxiety disorders are considered poor candidates for standard therapy with anti-anxiety drugs of the benzodiazepine class because these drugs can cause a second addiction.

NIDA-supported researchers have identified effective ways to tailor treatment for some patients with dual diagnoses. In one study, opiate addicts with APD responded better when standard contingency

management therapy was modified. In the standard type of this therapy, patients receive small rewards for abstinence that become progressively greater the longer abstinence is maintained. In the modified version, treatment professionals gave more frequent rewards for desirable behaviors, such as attending scheduled counseling sessions and testing clean for drugs. (See "Specialized Approach Shows Promise for Treating Antisocial Drug Abuse Patients," V11-4, September/October 1996.) In another study, drug craving was reduced among teenage cocaine abusers with bipolar disorder who receive lithium, and in depressed heroin abusers who were treated with imipramine. (See "Treating Mood Disorders in Drug Abuse Patients," V13-6, March 1999.) In this issue of *NIDA NOTES*, we report on promising results with methylphenidate and antidepressants in children with attention-deficit/hyperactivity disorder (ADHD) and

with methylphenidate in adult cocaine abusers with ADHD. (See "Medication Reduce Incidence of Substance Abuse Among ADHD Patients.")

Just as the co-occurrence of drug abuse and mental health problems presents special problems for treatment, so does it also for research. The problems arise in part because drug abuse and other mental health disorders can intertwine in several ways. For example, successful treatment of cocaine addiction often also dispels concurrent depression, while nicotine addicts' depression commonly persists after successful smoking cessation treatment. Such variations make it difficult to generalize treatment research findings across large patient groups.

As a result, progress has been made in relatively small increments. Another problem facing researchers is that a study population that is ostensibly uniform because all individuals have the same drug abuse and mental health disorders may actually be nonuniform. The reason is that the relationship between the two disorders may vary in different patients. For example, some people with a mental disorder may initiate drug use as an inappropriate form of self-medication, some people who take drugs may develop mental disorders as a consequence of their drug use, and a third group may simply have the two disorders at the same time. If an intervention is evaluated in a study population where some patients have drug abuse as a primary disorder and others as a secondary disorder, the treatment may appear to be ineffective even though it works well for one of these subgroups.

A structural difficulty that complicates research on drug abuse and mental illness comorbidity is that few drug abuse treatment programs treat enough patients with a particular mental health disorder to easily generate the

preliminary data necessary to justify a full-scale study of a treatment for the disorder. To overcome this difficulty and

accelerate the pace of discovery, NIDA's Behavioral Therapy Development Program places special emphasis on pilot studies in drug abuse and mental illness comorbidity. The program represents a kind of research "venture capital," making possible the rapid initial testing of many ideas, the best of which will then proceed rapidly to further, more definitive testing. Starting next year, NIDA's Clinical Trials

Network will accelerate this wider testing by facilitating the recruitment of large numbers of patients with the drug abuse and comorbidity characteristics that treatments are designed to address. (See "Clinical Trials Network Will Speed Testing and Delivery of New Drug Abuse Therapies," V14-1, April 1999.)

Drug abuse and mental health professionals both confront the difficulty of providing effective care to patients whose problems overlap two health care specialties that share much, but are also in many ways very distinct. In response to this situation, NIDA and the National Institute of Mental Health have been actively collaborating on epidemiologic and treatment research on comorbidity. For example, the two Institutes are examining the problem of treating the relatively small population of patients who abuse drugs and also have severe mental disorders, such as schizophrenia or bipolar disorder. These patients require integrated specialty treatments.

In drug abuse as in other areas of health care, isolated disorders are simplest to study and treat, but comorbidity is reality for many individuals. NIDA research has laid the foundation for successful investigations of these complex realities. **NN**

Drug abusers who have concurrent, or comorbid, mental health problems are at the top of the list of those who will benefit from this research.

Clinical Trials Network Will Speed Testing and Delivery Of New Drug Abuse Therapies

By Patrick Zickler, *NIDA NOTES* Staff Writer

Over the past quarter century, NIDA research programs have produced dramatic advances in understanding drug abuse and addiction and led to the development of an array of new treatments and therapies to help patients with drug abuse problems. But, in order to fulfill their promise, the advances achieved in drug abuse research centers must reach patients in the community-based settings where most treatment is provided. To enhance the delivery of scientifically based treatments to drug abuse patients, NIDA is establishing the National Drug Abuse Treatment Clinical Trials Network.

The Clinical Trials Network (CTN) will provide a structured partnership in which NIDA, treatment researchers, and community-based service providers will cooperatively develop, validate, refine, and deliver new treatment options to patients in community-level clinical practice.

"The Clinical Trials Network is a revolutionary advance in the study and treatment of drug abuse and addiction. It is the most important initiative the Institute has ever undertaken," says NIDA Director Dr. Alan I. Leshner.

The CTN framework will consist of Regional Research and Training Centers (RRTC) linked in partnership with 5 to 10 or more community-based treatment programs (CTPs). These RRTC/CTP partnerships will constitute CTN Research Nodes. "Each Node will include CTPs that represent a variety of patient populations and will be linked through the Network with other Nodes throughout the country," says Dr. Stephen Zukin, director of NIDA's Division of Clinical and Services Research. "This means the Clinical Trials Network will provide a broad and powerful infrastructure for rapid multisite testing of promising science-based therapies. Patients in community-based treatment settings across the country will benefit, and benefit sooner, from well-developed science-based care."

The CTN will be national in scope but anchored on community-level programs. The size and diversity of patient populations participating in CTN studies will provide a resource for concurrent testing of promising therapies and will make it possible to conduct comprehensive investigations

of factors such as environmental and genetic determinants of vulnerability to drug dependence and abuse. CTN investigators and treatment providers and others in the broader research community will have access to the research database generated by the CTN.

The CTN will help meet one of the principal needs identified in *Bridging the Gap Between Research and Practice*, the Institute of Medicine's 1998 report on community-based drug and alcohol treatment. The report recommended the development of an infrastructure to facilitate research within a network of community-based treatment programs. NIDA announced its intention to establish the CTN in December 1998, and has issued a Request for Applications soliciting cooperative agreement applications from established clinical investigators to participate in the Clinical Trials Network.

NIDA has committed first-year funding of \$10 million for the CTN. The Institute plans to make as many as four awards, for project periods up to 5 years, during the first year. When fully developed, the Network will include from 15 to 30 Nodes incorporating well over 100 community treatment facilities.

The CTN partnership is designed to meet a range of objectives that include:

- supporting studies of behavioral, pharmacological, and combined behavioral and pharmacological treatment interventions of proven efficacy in rigorous, multisite clinical trials to determine effectiveness across a broad range of treatment settings and patient populations;
- furthering the development of effective treatments by integrating behavioral, pharmacological, and treatment research;
- investigating the impact of advances in treatment research on community-level treatment practices;
- ensuring that treatment research in drug abuse and addiction meets the needs of the wider community, including minorities, women, children, and underserved populations;

-
- fostering the collaboration of community treatment practitioners and researchers to provide opportunities for exchange of ideas, information, and values between the treatment and academic communities; and
 - determining the impact of the transport of novel, effective treatments in the community on the incidence and prevalence of various other illnesses and conditions, including HIV and hepatitis.

For More Information

Additional information about the Clinical Trials Network is available through NIDA's home page on the World Wide Web at <http://www.nida.nih.gov/> by clicking on the Clinical Trials Network 

Antistress Medications May Help Drug Abuse Patients Avoid Relapse

A class of medications currently being developed by several pharmaceutical companies may help drug abuse patients avoid relapse after experiencing stress. Called CRF antagonists, the compounds block the action of corticotropin-releasing factor (CRF), a naturally occurring chemical in the brain. Scientists think that CRF may play a key role in producing arousal, anxiety, and other emotional responses to stress.

Dr. Yavin Shaham, formerly of the University of Toronto and now in NIDA's Intramural Research Program in Baltimore; NIDA grantee Dr. Jane Stewart of Concordia University in Montreal; and their colleagues at Concordia University and the Addiction Research Foundation in Toronto have conducted a series of studies to determine whether CRF antagonists can prevent stress-induced relapse to drug-seeking in rats. In these studies, rats were trained to press a lever to receive a dose of cocaine or heroin. After the rats learned this behavior, the supply of drugs was terminated so that pressing the lever no longer resulted in a dose of drug. As a result, the rats reduced their lever pressing to practically nothing. However, when the rats were given mild intermittent footshocks for 10 to 15 minutes, they started to press the lever again as soon as it became available, even though they did not receive any drug. This indicates that stress can reinstate drug seeking in rats, just as it is reported to do in human addicts, says Dr. Stewart.

The researchers found that giving the rats a CRF antagonist prior to giving them footshocks could greatly reduce the rate at which the rats would press the lever again. However, the compound had no effect when the rats were pressing a lever to receive a drop of sugar solution that they could drink. "This suggests that the CRF antagonist blocks stress-induced relapse to drug seeking specifically and does not produce its effects by interfering with the animal's ability to press the lever," says Dr. Stewart.

Results such as these have interested staff in NIDA's Medications Development Division (MDD) in the potential of CRF antagonists for treating drug abuse relapse. "What's so interesting about CRF antagonists is that evidence suggests that they may be useful in treating relapse to a variety of drugs, including cocaine, heroin, and nicotine," says Dr. Jane Acri of MDD. "This is particularly important considering that people who abuse drugs often abuse a number of different drugs."

Source

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Treating Mood Disorders in Drug Abuse Patients Yields Improvement in Both Conditions

By Patrick Zickler, NIDA NOTES Staff Writer

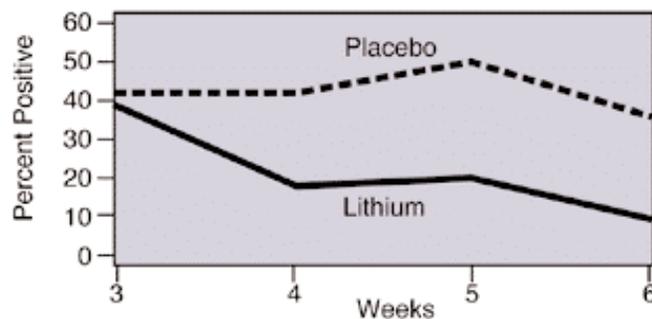
For many drug abuse patients, mood disorders are a constant companion. Among cocaine abusers, for example, depressive disorders are the most commonly diagnosed coexisting, or comorbid, conditions. The relationship between mood disorders and drug abuse in these patients is often complex and interconnected: Drug abuse patients may develop depression as a result of the physical and psychological suffering associated with their drug use, and patients suffering from mood disorders may become drug dependent in attempts to self-medicate. For patients suffering from both drug abuse and mood disorders, the conditions once seemed impossible to untangle, but recent NIDA research suggests that treatment for the mood disorder alone also can have a positive effect on drug abuse treatment.

One NIDA-supported study found that drug use declined among teenage drug dependence patients being treated with a medication for bipolar disorder, which is characterized by alternating periods of depression and mania. In a related study, chronic opiate-dependent adults reported less drug abuse when they were treated with the antidepressant imipramine for comorbid depression.

Reducing Substance Dependence in Bipolar Teens

Lithium has proven effective in treating adult bipolar disorder patients and research with adult patients suggests that lithium also may be an effective treatment for comorbid substance dependence. However, no double-blind, placebo-controlled studies have tested the therapy in adolescents. Now, at Washington University in St. Louis, Dr. Barbara Geller and her colleagues have found that,

PERCENT OF URINE SAMPLES POSITIVE FOR DRUGS: PATIENTS TAKING LITHIUM VS. PATIENTS TAKING A PLACEBO



Random weekly urine analysis showed significantly lower drug use among patients who received lithium compared with patients who received a placebo.

in adolescent patients, lithium treatment for the manic phase of bipolar disorder also reduces drug and alcohol dependence.

The researchers' double-blind, placebo-controlled study involved 25 teenage patients who had been diagnosed with bipolar disorder and secondary substance abuse disorder involving marijuana, alcohol, inhalants, or multiple drugs. "Most of these kids have had bipolar disorder since the age of 9,"

Dr. Geller says. "They have been severely ill for a long time, and most are from families with a history of bipolar disorder."

More than half of the patients also came from families with a history of substance abuse, sometimes reaching back several generations. All had begun using drugs in the year prior to being enrolled in the study. "Secondary substance dependence disorders are the most common and most severe comorbidity in bipolar patients," Dr. Geller says. "We wanted to get to them within the first year, when they were newly addicted."

All participants in the study received packets of capsules to be taken twice each day during the 6-week study. For half the teenagers, the capsules contained lithium dosages that have proven effective in treating adult bipolar patients. The other patients received placebo only. All participants, who were treated as outpatients, also received weekly therapy sessions. Blood levels of lithium were checked twice each week—once randomly—to make sure the participants were taking the pills. Urine samples were collected twice weekly—once randomly—to monitor drug use.

The percentage of drug-positive urine samples for participants receiving placebo remained essentially unchanged, at roughly 40 percent, throughout the study. But for the

group receiving lithium, drug-positive urine samples dropped from 40 percent to approximately 10 percent. "We tested randomly six times during the study and the urine samples confirmed the patients' self-reports. There was a significant decrease in drug use," Dr. Geller says.

In addition, patients in the lithium group showed significantly greater improvement in symptoms of bipolar disorder - such as their ability to function in family, school, and social settings - than did those receiving a placebo.

"Lithium treatment of bipolar disorder in adolescents with secondary substance dependence disorders was an efficacious treatment for both disorders," Dr. Geller concludes.

Reducing Craving in Methadone Patients

Dr. Edward Nunes and his colleagues at the New York State Psychiatric Institute and Columbia University College of Physicians and Surgeons in New York City found that antidepressants used to treat comorbid depressive disorders in adult methadone treatment patients not only can improve their mood but also reduce their craving for drugs.

"We were able to identify and treat primary or secondary depression in chronically drug-dependent adults," Dr. Nunes says. "In some respects, treating depression as a separable disorder represents a sea change in the way we look at comorbidity in these patients."

In Dr. Nunes' study, patients receiving imipramine to treat depression showed substantial drops in depressive symptoms, and many patients whose depressive symptoms improved also reported decreased craving and use of drugs, including opiates, cocaine, and marijuana.

"There is evidence that treating the depression helps some patients take advantage of therapy and could be successful as one part of treatment," Dr. Nunes says.

The 12-week study involved 137 patients recruited from 2 community-based methadone maintenance programs. Patients also were diagnosed with primary depression that predated their drug use or secondary depression that emerged or persisted through a period of abstinence or had lasted for at least 3 months during a current period of drug use. Patients were randomly assigned to either imipramine or placebo. Eighty-four patients completed at least 6 weeks of the trial. Fifty-seven percent of patients receiving imipramine were rated as having substantial improvement in both mood and drug use compared with only 7 percent among the patients receiving placebo. Fourteen percent of patients receiving imipramine achieved abstinence, confirmed by urinalysis, for 4 weeks compared with 2 percent of patients who received placebo.

"Imipramine had a very robust and positive effect on mood. This improved mood was associated with less intense and less frequent drug craving and, to a lesser extent, with reduced drug use," Dr. Nunes says.

Sources

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Coping Skills Help Patients Recognize and Resist The Urge to Use Cocaine

By Patrick Zickler, NIDA NOTES Staff Writer

For some cocaine abusers, urges to use cocaine come out of the blue. But more often the urge is associated with an identifiable situation that triggers drug use. A behavioral science research study supported by NIDA has led to the development of a treatment technique that helps cocaine users control their drug use by recognizing and coping with these high-risk situations.

Dr. Damaris Rohsenow, Dr. Peter Monti, and their colleagues at Brown University's Center for Alcohol and Addiction Studies in Providence, Rhode Island, have developed a cocaine-specific coping skills training (CST) technique that can be used as part of a treatment program to help cocaine abuse patients identify situations that trigger their urges to use cocaine and modify their behavior to avoid drug use.

In the study, patients who received CST as part of treatment "had significantly shorter and less severe relapses during the 3-month followup period than did patients who received standard treatment," Dr. Rohsenow says.

Patients who received CST were taught to identify high-risk situations, called triggers, associated with drug use. These triggers were broadly categorized into topic areas such as anger, money, frustration, or depression. Patients then focused on specific personal examples of triggers and analyzed the sequence of actions, called a "behavioral chain," that led to drug use in those situations.

Patients learned how to avoid or modify the trigger situation when possible. "For example, if a money trigger is associated with getting a paycheck, they might arrange for their paycheck to be directly deposited in their bank. Or if drug use is associated with their lunch break, patients could eat with a group of coworkers rather than going out alone," Dr. Rohsenow explains.

For situations in which the trigger could not be avoided, patients developed a repertoire of cognitive and behavioral skills to modify the behavioral chain and reduce their personal risk of drug use. "A phone call from an ex-spouse might be an 'anger' trigger that can't be avoided. But patients can use coping skills training to change how they behave in response to the call. They can 'talk out' their

Coping skills training can help patients identify situations that trigger their urges to use cocaine and modify their behavior to avoid drug use.

anger with friends or do something physical like go out and play basketball," Dr. Rohsenow says.

The study involved 128 male and female patients selected from 2 drug abuse treatment facilities. Standard treatment at these facilities is an abstinence-based program that combines the principles of the Alcoholics Anonymous 12-step program with educational information presented in group formats, individual counseling sessions, and family or marital therapy.

Roughly half the patients received standard treatment plus eight 1-hour sessions of

CST. The other half received standard treatment plus eight 1-hour sessions of meditation-relaxation training (MRT), a procedure that often is used as part of treatment programs but has no significant effect on substance use. The MRT procedure assured that all patients in the study spent the same amount of time in contact with therapists.

The patients were evaluated at 1 and 3 months following treatment. Roughly 45 percent of patients from each group suffered relapses following treatment, but relapsing CST patients averaged only 6.2 days of drug use compared with more than 13 days of cocaine use for patients who received MRT.

The improvement in outcome for most CST patients was far better than these average figures suggest, Dr. Rohsenow points out, because one relapsed CST patient used cocaine for 49 out of 90 days in the followup period. The other CST patients averaged only 3.8 days of drug use.

Among CST patients, the longest binges averaged 2.8 days - less than half as long as the binges for the other patients, which lasted an average of 6 days.

"Patients with CST training were able to change the way they thought and then change the way they behaved in situations that posed a risk of relapse," Dr. Rohsenow says.

Source

- Monti, P.M.; Rohsenow, D.J.; Michalec, E.; Martin, R.A.; and Abrams, D.B. Brief coping skills treatment for cocaine abuse: substance use outcomes at three months. *Addiction* 92(12): 1717-1728, 1998. **NN**

Matching Drug Abuse Treatment Services to Patient Needs Boosts Outcome Effectiveness

By Neil Swan, NIDA NOTES Staff Writer

Matching a drug abuse treatment patient with the right type of treatment program is a much-discussed but elusive goal for drug abuse treatment providers. In the real world, a patient simply may not have the option of switching to another treatment program that might be a better match for his or her needs. For example, a patient's choices may be limited by the insurers, employers, or Government programs that pay for the treatment.

Even within these limitations, however, treatment needs can be evaluated and special services can be targeted to meet patients' specific needs with effective outcome results, NIDA-funded research shows.

Dr. Thomas McLellan and his colleagues at the University of Pennsylvania in Philadelphia first sought to develop and evaluate a clinically practical matching procedure for assigning patients to treatment programs that were deemed most appropriate to the patients' needs. But the investigators could find no evidence of better outcomes for any particular type of patient, regardless of whether

the assigned program was inpatient or outpatient. The researchers also found that insurance coverage requirements made it difficult to place patients in selected treatment programs even when the patients were willing to go to that program.

So the researchers redirected their goal from "matching patients with programs" to "matching patients' problems with targeted therapy services" furnished within the treatment program that was covered. They compared outcomes of patients in matched-services programs to outcomes of patients receiving standard, unmatched services, in four private treatment programs in Philadelphia - two inpatient and two outpatient programs. The 94 adult patients in the study all were employed and were dependent on drugs, alcohol, or both. All treatment costs were covered by employer-provided insurance.

On entering treatment, patients were interviewed using the Addiction Severity Index (ASI), a standard hour-long interview designed to measure severity of problems in the

CHANGES IN THE ADDICTION SEVERITY INDEX VARIABLES

	On Entering Treatment	6 Months After Discharge	On Entering Treatment	6 Months After Discharge
PROBLEMS NOT TARGETED				
Days of Alcohol Use	12	2	15	1
Days of Alcohol Intoxication	11	2	13	1
Days of Opiate Use	3	1	1	1
Days of Cocaine Use	4	1	5	1
Days of Medical Problems	4	5	3	3
TARGETED PROBLEMS				
Days Worked	16	14	14	17
Employment Income	\$1,318	\$1,072	\$1,042	\$1,435
Days of Family Problems	4	4	3	1
Days of Psychological Problems	10	7	11	4

Variables reflect the 30 days prior to treatment admission and 6-month followup.

NIDA Research Provides Data to Document and Improve the Effectiveness of Drug Abuse Health Services

NIDA Director Dr. Alan I. Leshner

As part of its mission to treat and prevent drug abuse and addiction, NIDA has supported the development of numerous research-based drug abuse treatment protocols and drug abuse prevention models. In keeping with standard scientific methodology, these programs have been tested in tightly controlled practice settings with carefully selected populations.

Once these programs are tested the critical question becomes: Will the promising treatment outcomes produced in a controlled research environment hold in widely varying real-life treatment settings and for a wide range of patients? Likewise, will the prevention model that worked on a small scale continue to work in communities that may vary in any number of factors from size and ethnic composition to geography and the nature of their school systems?

To answer these questions, NIDA supports an extensive and growing portfolio of health services research. That portfolio is designed to give drug abuse treatment and prevention service providers the scientific data and research-based methodologies they need to gauge and enhance how well their programs will work for real-life patients in real-life settings. NIDA's health services research also encompasses economic analyses that provide answers to questions such as: Does this drug abuse program provide effective services that are accessible to patients at a reasonable cost? How does this program compare to similar programs in terms of its cost-effectiveness and accessibility? Does this program not only reduce drug abuse and addiction, but also reduce costs to society from drug-related crimes and health expenditures?

While much remains to be done, NIDA-funded scientists have built a solid foundation of science-based information that can be used to document and improve the effectiveness of drug abuse health services. Much of the Institute's research in this area is conducted at its health services



Will the promising treatment outcomes produced in a controlled research environment hold in widely varying real-life treatment settings and for a wide range of patients?

research centers, which investigate the Nation's pressing drug abuse health services issues.

For example, investigators at the Center for Managed Care and Drug Abuse at Brandeis University in Waltham, Massachusetts, and Harvard University in Cambridge, Massachusetts, are assessing the impact of managed care on drug abuse treatment availability, content, duration, and utilization. They also are studying how managed care affects the organization and financing of drug abuse treatment facilities. At the Community-Based Health Services Research Center on Chronic Drug Users at the University of Miami in Florida, researchers are using the Dade County, Florida, health services system as a case study to find ways to improve drug abuse patients' access to both primary medical care and drug abuse treatment. The investigators are exploring how the Dade County system identifies, assesses, and serves chronic drug users, and, in particular, whether health care access and effectiveness vary by ethnicity or gender.

The Institute has supported three nationwide studies to assess the effectiveness of drug abuse treatment using numerous measures of treatment outcomes. All three studies have shown that drug abuse treatment patients in the four most common types of treatment programs - outpatient methadone, outpatient nonmethadone, long-term residential, and short-term inpatient - dramatically reduce their drug use following treatment, reduce drug-related criminal activities, and improve their physical and mental health. (For results of the most recent study—the Drug Abuse Treatment Outcome Study—see *NIDA NOTES*, V12-5, September/October 1997.)

These studies and other NIDA-funded research highlight the value of providing patients with services in addition to drug abuse treatment. A recent study at the Treatment

Research Institute in Philadelphia has found that providing drug abuse patients with services based on their needs in three areas—employment, family relations, and psychiatric problems—can boost the effectiveness of treatment. (See “Matching Drug Abuse Treatment Services to Patient Needs Boosts Outcome Effectiveness.”)

NIDA-funded studies on the economics of treatment and prevention services are comparing the costs of drug abuse services with measures that can be quantified in dollar amounts, such as reduced costs of crime and avoided costs for medical consequences of drug use. Other such studies compare the costs of drug abuse services with measures that cannot be quantified in dollar amounts, such as how long a patient remains abstinent or a patient's degree of social functioning. These studies consistently show that resources spent on drug abuse services result in substantial savings to society. For example, results from the Midwestern Prevention Project—a comprehensive, NIDA-funded prevention study that was conducted in Kansas City, Kansas; Kansas City, Missouri; and Indianapolis, Indiana—indicated that every dollar spent on prevention programs saved \$68 per affected family in health and social costs.

To help treatment providers improve treatment outcomes and reduce costs, NIDA is developing a manual to guide them in conducting economic analyses on their own programs. The new manual—titled *Measuring and Improving Cost, Cost-Effectiveness, and Cost-Benefit for Substance Abuse Treatment Programs*—will provide managers with step-by-step procedures for analyzing the costs of their services and for producing economic analyses. These analyses will provide valuable insights into how providers can serve

An economic analysis of the Midwestern Prevention Project indicated that every dollar spent on prevention programs saved \$68 per affected family in health and social costs.

their patients more efficiently. In the future, the economic data generated by treatment providers throughout the country may be pooled by researchers to produce further large-scale economic studies of drug abuse treatment, which, in turn, will give policymakers and insurance companies more science-based information to help them make decisions related to financing drug abuse treatment. In the coming months, the manual will be available both in print and on NIDA's home page on the World Wide Web. The Web site will also enable treatment providers to communicate with each other about the manual and their findings.

To keep pace with rapid advances in health services research, NIDA regularly evaluates its health services research agenda by drawing on resources both in the drug abuse field and in the health services research field at large. In December 1997 the Institute began hosting a series of meetings intended to help define an agenda for health services research. These meetings culminated in a research symposium at the annual conference of the Association for Health Services Research in June. (See “Reserachers at NIDA Symposium Discuss New Directions for Health Services Research.”) We will use the information and ideas gleaned from these meetings in the coming months as we develop plans for advancing our research to improve health services for drug abusers.

We must press forward in our search to find ways to provide quality treatment to all drug abuse patients at reasonable costs. Likewise, we must continue to work to insure that promising drug abuse prevention research findings translate to real reductions in drug use among our Nation's children. **NN**

Men and Women in Drug Abuse Treatment Relapse at Different Rates and for Different Reasons

By Steven Stocker, *NIDA NOTES* Contributing Writer

Recent NIDA-funded studies have found that women in drug abuse treatment relapse less frequently than men do, at least partly because women are more likely to engage in group counseling. Other NIDA-supported researchers have found that cocaine-addicted women and men differ in the factors that cause them to relapse, indicating that males and females might benefit from different relapse prevention strategies.

Likelihood of Relapse

In a study conducted at the University of California, Los Angeles, Dr. Robert Fiorentine and his colleagues have found that women drug abusers are less likely than men drug abusers to relapse after entering treatment because women participate more frequently in group counseling and that this more intensive level of treatment engagement helps them to remain drug-free.

The researchers followed 182 women and 148 men in 26 public outpatient drug abuse treatment programs in Los Angeles County. The programs provided group, individual, and family counseling; educational activities; and referrals to other health and social services. The treatment lasted 6 months.

About half the patients regularly used just one drug—primarily crack cocaine, marijuana, or powder cocaine, and about half used more than one drug. Regular use was defined as three or more times per week. The patients were interviewed while in treatment and approximately 6 months after the first interview.

The scientists found that the women in their sample were less likely than the men to relapse: only 22 percent of the women compared to 32 percent of the men relapsed to drug use in the 6 months between interviews. The researchers considered several theories to account for this finding.

One possibility was that the women used drugs less than the men, so abstaining from drug use was easier for them. However, the study findings showed otherwise. In the year preceding treatment, more women had used crack cocaine than men, and about the same percentages of women and men had used powder cocaine, marijuana, and other drugs. In addition, women used all drugs as frequently as men, except for crack and heroin, which women used more frequently. Finally, about the same percentage of women and men used two or more drugs.

Another possibility the researchers considered was that the women received more social support than the men from a variety of sources, such as families, friends, and coworkers. The investigators found that, although the women were more likely than the men to maintain a social network, they were no more likely than men to receive emotional support for their problems and encouragement to stop using drugs.

What did appear to explain the difference in relapse was the fact that the women were more likely to engage in treatment, particularly group counseling, says Dr. Fiorentine. In his study, the women engaged in an average of 10.9 sessions of group counseling per month compared to 7.9 sessions a month for the men. Research has shown that more intense participation in treatment is associated with lower rates of relapse.

The women did not seem to be attending group counseling sessions more often than men because the sessions were somehow oriented more toward women. The sessions dealt with the problems of both genders more or less equally and were usually attended by both men and women, Dr. Fiorentine says.

The reason that women attended group counseling sessions more than men may stem from women's greater willingness to seek professional help for their health problems, speculates Dr. Fiorentine. "Women appear to be more willing to seek help for their problems, including their substance abuse problems," he says. "Men, on the other hand, are more likely to say, 'I'm OK. I don't need help. I can take care of this. It's just a little problem.'" He recommends that treatment providers discuss with male drug abusers the possibility that their reluctance to seek help may be hampering their recovery.

Even though the women attended more group counseling sessions than men, they did not attend more individual counseling or family counseling sessions than men did. If women are more likely to use services in general, why did they not engage more often in these other types of therapies? The explanation seems to be that these other therapies are not offered as frequently as group counseling in Los Angeles County, primarily because of the county's budget constraints, Dr. Fiorentine suggests. "Individual counseling, for example, is expensive and there are only so many counselors to go around, so treatment programs ration individual counseling," he says.

"Both women and men already may be attending the maximum number of individual counseling sessions they can attend. If patients could attend as many of these sessions as they desired, you might see more women than men in these sessions, just as you see more women than men in group counseling sessions."

In a related study, Dr. Roger Weiss and his colleagues at McLean Hospital in Belmont, Massachusetts, also found less likelihood of relapse for women than for men among patients who were hospitalized for cocaine addiction. When 74 patients were interviewed 6 months after the hospitalization, 51 percent of the women had remained abstinent compared to 25 percent of the men.

Like Dr. Fiorentine, Dr. Weiss theorizes that the women in his sample were more motivated for therapy than the men were. "Studies have identified barriers to entering drug abuse treatment programs that exist for women but not for men," says Dr. Weiss. "These include childcare difficulties and the predominance of male patients and staff. There is also more social stigma for women in being labeled an addict. Women who come to these treatment facilities must be willing to overcome these barriers, which could lead to a higher percentage of women who are motivated to change."

Reasons for Relapse

In addition to identifying gender differences in the likelihood that drug abusers relapse, scientists also have identified gender differences in drug abusers' experiences before and during relapse. Dr. James McKay and his colleagues at the University of Pennsylvania in Philadelphia found that women in treatment for cocaine addiction were more likely than men to report negative emotions and interpersonal problems before they relapsed. The men, on the other hand, were more likely to report positive experiences prior to relapsing and were more likely to engage in self-justification and rationalizing afterward. They reported, for example, that they felt entitled to use cocaine or that they believed they could control their cocaine use. The women also were much more likely to be impulsive in their return to cocaine use. Fifty-six percent of the women, compared with only 17 percent of the men, reported that they relapsed immediately after the thought of using cocaine occurred to them.

These gender differences in relapse factors suggest that different relapse prevention strategies might be emphasized for women and men, says Dr. McKay. For example, women might benefit more from techniques that enable them to deal more effectively with unpleasant emotions and interpersonal problems. "One strategy is to take action quickly as your mood starts to deteriorate rather than waiting until you are in a really bad mood and then trying to do something about it," he says. "If it's a small

problem, planning an enjoyable activity might be all that is needed. If, however, it's a serious depression, medication or psychotherapy might be necessary."

In contrast, men might benefit more from strategies that counter their tendency to let down their guard when feeling good, Dr. McKay says. "These strategies are derived from concepts taught in 12-step programs, such as not getting too cocky or confident when your mood improves," he says. "Patients are told to be on the lookout for warning signs that might be present when they're feeling good, such as thinking to themselves, 'I'm feeling great today. I don't need to go to that meeting. I can go hang out with this friend of mine. I know he uses, but I'm feeling good today, and I'm not vulnerable to using.'"

More Research

Gender differences in drug abuse are of intense interest to NIDA, says Carol Cowell of NIDA's Division of Clinical and Services Research. "Researchers are finding gender differences across the broad spectrum of drug abuse research—from basic research to studies such as these on treatment and services—and we would like to encourage more study of these differences," she says. She occasionally suggests that NIDA-funded researchers analyze their data in terms of gender differences. "This sometimes results in a study that increases our knowledge of the role of gender in treatment outcomes," she says.

"Performing gender analyses is simply a matter of doing good science," says Dr. Cora Lee Wetherington, NIDA's women's health coordinator. When gender differences exist but investigators fail to test for them, flawed conclusions may be drawn, either for males or females or both, she says.

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Drug Addiction Treatment Conference Emphasizes Combining Therapies

By Steven Stocker, *NIDA NOTES* Contributing Writer

Drug addiction can often be treated best through a combination of behavioral and pharmacological treatments and social service interventions, according to speakers at NIDA's National Conference on Drug Addiction Treatment. The conference, held in Washington, D.C., in April, attracted more than 800 drug abuse treatment researchers and service providers, leaders of professional organizations, criminal justice and law enforcement personnel, representatives from State drug abuse agencies, and public policymakers. The conference was presented as part of NIDA's Treatment Initiative, which is designed to improve the quality of the Nation's drug abuse treatment. (See "NIDA Launches Drug Abuse Treatment Initiative," V12-4, July/August 1997).

Research is showing that drug addiction therapy that combines different approaches is often more effective than therapy that uses only one approach, said NIDA Director Dr. Alan I. Leshner. "When all is said and done, the ultimate cure for drug addiction will probably involve a combination of biological and behavioral treatments and social services," he said.



At the conference, Dr. Mary Jeanne Kreek of Rockefeller University describes the health benefits of methadone treatment combined with behavioral treatments.

This approach of treating drug addiction by combining biological and behavioral therapies stems in part from studies showing that addiction is both a biological and a behavioral disorder, Dr. Leshner said. "What science has taught us is that drug addiction is a result of an interaction between an individual's biological vulnerability plus his or her experiences plus environmental factors plus, of course, drugs. The final result is a changed brain," he said. Viewing drug addiction as exclusively biological or behavioral is too limiting, he cautioned. "Let us not pit biology against behavior. These are not opposing viewpoints."

Combining medications with behavioral treatments can have an additive effect on therapy because the different treatments work on different aspects of addiction, said Dr. Bruce Rounsaville of Yale University in New Haven, Connecticut. Medications, such as methadone or medications that treat psychiatric disorders, can increase the chances that patients will stay in treatment. Psychotherapy can then help motivate patients to abstain from drugs and help them develop healthier lifestyles, said Dr. Rounsaville. Several speakers examined behavioral therapies that are proving effective in treating drug addiction.

Dr. Kathleen Carroll of Yale University School of Medicine described cognitive-behavioral therapy (CBT), a comparatively brief intervention that helps cocaine-dependent individuals become abstinent from cocaine and other substances. In CBT, patients learn to recognize and avoid the situations in which they are most likely to use cocaine. They also learn how to cope with their urges to use cocaine and to deal with their psychological, occupational, and other problems. "Drug use requires skills involving getting the money to buy drugs, getting the drugs, and other activities," said Dr. Carroll. "In CBT, the patient learns that he or she has the capacity to learn skills that are healthier and more productive," she said.

Another effective behavioral approach involves rewarding patients for staying abstinent, according to Dr. Maxine Stitzer of Johns Hopkins University in Baltimore. For example, patients can be given vouchers as a reward for drug-free urines. The vouchers can be exchanged for healthful goods or services valued by the patients.

In family therapy for drug addiction, the therapist suggests ways that family members can help their addicted relatives stop abusing drugs, said Dr. José Szapocznik of the University of Miami School of Medicine in Miami, Florida. In one situation, for example, a mother ordinarily may allow her adult drug-abusing daughter to stay with her for several days in between drug binges, despite her misgivings about the daughter's drug abuse. In family therapy, the therapist might encourage the mother to set limits for her daughter, such as allowing her to stay only if she agrees to remain abstinent. In addition to helping an addict, family therapy also has the potential for reaching other members of the family who may themselves have problems with drug abuse, said Dr. Szapocznik.



At NIDA's treatment conference, Dr. Kathleen Carroll of Yale University describes how cognitive behavioral therapy can help patients learn to avoid situations in which they are likely to use cocaine.

Dr. Herbert Kleber of Columbia University in New York City reported on detoxification techniques that help opiate addicts cope with withdrawal symptoms when they stop using opiates. Newer techniques include the use of a combination of the opiate treatment medications buprenorphine, clonidine, and naltrexone and the use of anesthesia or heavy sedation. Detoxification is only the first step in treating opiate addicts, Dr. Kleber stressed. "You should measure success not only by the level of comfort during withdrawal but also by how many patients go on for further therapy," he said.

Other speakers discussed the challenges of providing drug abuse treatment for special populations. For example, individuals with both severe mental disorders, such as schizophrenia, and drug abuse disorders should be treated for both conditions concurrently, said Dr. Robert Drake of Dartmouth Medical School in Hanover, New Hampshire. This is best accomplished by multidisciplinary case management teams that might include a psychiatrist, a mental health case manager, a substance abuse specialist, and a vocational specialist who can address the patient's needs in an integrated fashion. This approach yields a

number of benefits, including fewer relapses and hospitalizations and a higher functional status, said Dr. Drake.

Many drug-abusing adolescents also have a mental disorder, such as conduct disorder or depression, said Dr. Paula Riggs of the University of Colorado Health Sciences Center in Denver. These disorders contribute to the severity of the drug abuse disorder and should be treated concurrently, she said.

Drug abuse treatment can have health benefits in addition to reducing drug use, according to several speakers. Dr. David Metzger of the University of Pennsylvania in Philadelphia described numerous studies demonstrating that drug abuse treatment reduces the rates of HIV infection, by reducing both syringe sharing and risky sexual behaviors. Dr. Mary Jeanne Kreek of Rockefeller University in New York City presented data showing that, among injection drug users in New York City, methadone treatment, when combined with appropriate behavioral treatment, is reducing rates of both HIV infection and hepatitis B and, to a lesser extent, hepatitis C. Methadone treatment can also improve the health of addicts by normalizing immune function and the levels of stress and sex hormones, all of which are altered by drug abuse, Dr. Kreek said.

Thirteen million people in the United States currently abuse drugs, and 4 million are compulsive drug abusers, said General Barry McCaffrey, director of the Office of National Drug Control Policy, in the keynote address. The goal is to reduce the percentage of the U.S. population that is abusing drugs to under 3 percent by 2007, he announced. **NN**

Addiction Research Can Provide Scientific Solutions to the Problem of Cigarette Smoking

NIDA Director Dr. Alan I. Leshner

Every year, tobacco-related illnesses take the lives of more than 430,000 Americans. The force behind this grim statistic is the chronic, relapsing brain disease of addiction - in this case, addiction to nicotine. Only research on nicotine addiction can provide effective, science-based solutions to this costly public health problem.

More than two decades of NIDA leadership in addiction research have already provided much scientific information about addiction to nicotine. This research has led to the development of smoking prevention and treatment approaches that are helping to counter nicotine's threat to the public health today. NIDA-supported basic and clinical research promises additional improvements in treatment as scientists continue to unravel the mysteries of addiction to nicotine and other abused drugs.

Most smokers know that cigarette smoking and other forms of tobacco use are harmful. Nearly 35 million of them try to quit every year. Yet, without help, only a very small number actually are able to succeed. Science has shown why this is so. The nicotine in tobacco products is a highly addictive drug, and nicotine addiction is characterized by truly compulsive seeking and use, even in the face of harmful consequences.

Research on nicotine addiction has yielded a variety of pharmacological and behavioral treatments that have helped many people combat their nicotine addiction. For example, NIDA-supported research facilitated the development of nicotine replacement therapies, such as nicotine chewing gum and the transdermal nicotine patch, that enable many people to stop smoking. Yet, both research and extensive clinical experience have taught us that treating addiction with medication alone is not nearly as effective as when we couple the medication with a behavioral treatment. For example, we know that less than 10 percent of the people who try to quit smoking on their own are able to refrain from smoking for a year.



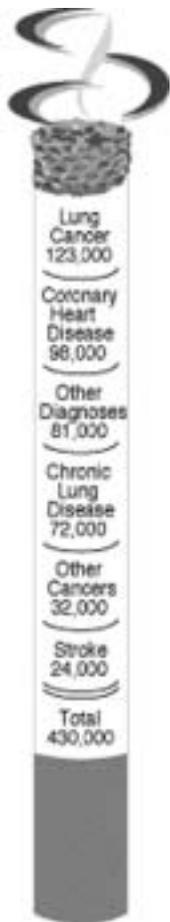
Research on nicotine addiction has yielded a variety of treatments that have helped many people combat their nicotine addiction.

Pharmacological treatments such as the patch and gum can double the odds of success. However, a combination of pharmacological treatment and behavioral treatment, such as group therapy or social support networks, can improve a smoker's chance of quitting even more.

NIDA's extensive behavioral research program is striving to increase the behavioral treatment options that clinicians can use with pharmacological treatments. Studies now under way are developing new, individualized behavioral treatments that will better motivate smokers to stop smoking and teach them techniques that will enable them to remain abstinent. Other treatment studies are testing whether currently available behavioral therapies, such as contingency management and relapse prevention, are more effective used alone or in combination to help smokers quit.

While we have made much progress in developing treatments for nicotine addiction, we can and must do more to help the many smokers who still are unable to quit smoking. I am happy to report that ongoing research by NIDA-supported scientists has been uncovering important new information about the nicotine addictive process and how that process drives smoking behavior. We can use these data to help us develop new treatments.

Two recent studies have confirmed inferences from earlier research that some of nicotine's most important effects on emotions and behavior are exerted through the same brain circuits that are activated by other abused drugs. One study shows that, like other drugs of abuse, nicotine elevates levels of the neurotransmitter dopamine in brain pathways that control reward and pleasure. This change in dopamine levels is thought to be a fundamental characteristic of all addictions. The second study shows that, as with withdrawal from other addictive drugs, withdrawal from chronic nicotine use decreases this brain circuit's sensitivity to pleasurable stimulation. Our increased



understanding of these changes shows us why it is so hard for people to stop smoking and helps pave the way to better treatments for nicotine withdrawal symptoms. (For more information on these and other nicotine studies, see "Like Other Drugs of Abuse, Nicotine Disrupts the Brain's Pleasure Circuit.")

***Every year, 430,000
deaths from cancer
and other diseases are
attributable to cigarette
smoking***

NIDA-supported researchers also are making excellent progress in identifying the molecular components of nicotine addiction. One recent study has pinpointed a particular protein in the brains of mice that is essential to the process of nicotine addiction. Mice that lack this protein will not self-administer nicotine. This suggests that the mice do

not experience the rewarding effects of nicotine. This major discovery provides us with a very specific brain site to target in developing novel nicotine addiction treatment medications.

Although nicotine addiction lies at the root of tobacco use, another recent study by scientists using sophisticated brain imaging technology suggests that, in addition to

nicotine, some unknown compound in cigarette smoke also raises dopamine levels in smokers' brains by inhibiting an enzyme that breaks down dopamine. If further research confirms that smoking alters dopamine levels through multiple mechanisms, it would open the door to new approaches to developing effective smoking treatment medications. (See "Tobacco Smoke May Contain a Psychoactive Ingredient Other Than Nicotine.")

Ultimately, the best treatment for nicotine addiction is prevention. Here, too, a long history of NIDA-supported research has given us the tools to develop effective drug abuse prevention approaches, including strategies to prevent tobacco use. We have distilled this scientific base for drug abuse prevention in the first-ever research-based guide for preventing drug abuse. The principles in this guide, "Preventing Drug Use Among Children and Adolescents," can be applied by families, schools, and communities to prevent adolescents from beginning to use tobacco and other harmful drugs. (See "NIDA Materials to Help Communities Develop Drug Abuse Prevention Programs," V12-6, November/December 1997).

Never before has the momentum for addressing the public health problem posed by tobacco use been greater. To accelerate this momentum, NIDA, in collaboration with the Robert Wood Johnson Foundation, the National Cancer Institute, and the Centers for Disease Control and Prevention Office on Smoking and Health, is holding a scientific conference on nicotine addiction on July 27-28, 1998, in Bethesda, Maryland. The conference, called "Addicted to Nicotine: A National Research Forum," brings together the leaders in nicotine addiction research to share knowledge, identify gaps in that knowledge, and point us toward promising new areas of research. Ultimately, it is that research that will make possible a future in which no more lives are lost to what is ultimately a preventable, and, if not prevented, treatable disease. **NN**

Innovative Treatment Helps Traumatized Drug-Abusing Women

By Neil Swan, NIDA NOTES Staff Writer

NIDA-funded researcher has developed an innovative treatment program to meet the special needs of drug-abusing women who also are diagnosed with posttraumatic stress disorder (PTSD), a disorder often associated with physical, sexual, or other abuse during childhood. PTSD victims re-experience their trauma, sometimes years later, through unexpected and recurring flashbacks or nightmares. The trauma that sparks PTSD may range from battlefield shock or childhood sexual molestation to violence related to drug dealing.

PTSD symptoms include "avoidant" behavior, which may be marked by loss of interest in favorite activities, avoidance or suppression of thoughts or emotions, feelings of detachment, or difficulty thinking about the distant future. PTSD victims may suffer increased arousal or anxiety, as shown in extra vigilance against perceived dangers, trouble concentrating, exaggerated responses to being startled, and outbursts of anger.

PTSD combined with drug abuse can be devastating for women struggling to survive in the street drug culture. One study, which evaluated women crack cocaine abusers with PTSD in New York City's Harlem, found that they are forced into vicious cycles in which they use crack to counteract the distress of trauma, suffer more drug-related trauma, and then turn to crack again.

Development of new treatment strategies for drug abusers with coexisting PTSD, especially women, should be a high priority, says Dr. Lisa M. Najavits of Harvard Medical School, who conducted a NIDA-funded review of research focusing on women with these problems. Treatments developed either for PTSD or substance abuse alone may not be sufficient, she says. Further, existing treatments for men with PTSD and drug abuse may not be directly applicable to women, she adds.

Dr. Najavits developed an innovative treatment program called "Seeking Safety" that consists of 24 sessions that teach women new coping skills to manage both disorders at once. Patients learn how to ask for help, set boundaries in relationships, nurture themselves, and fight cues and urges to relapse to drug use.

The safety theme is emphasized as the key to recovery from both PTSD and drug abuse.

"Safety" in this situation means abstaining from drugs and alcohol, reducing self-destructive behavior, establishing a network of supportive people, and guarding against the



Dr. Lisa Najavits of Harvard Medical School has developed an innovative treatment program for drug-abusing women with posttraumatic stress disorder resulting from traumas such as child abuse.

dangers associated with both disorders, such as HIV and domestic violence.

Of 27 women enrolled in the "Seeking Safety" program, 17 completed treatment. After treatment, these women showed significant reductions in drug use, trauma-related symptoms, suicide risk, and suicidal thoughts. They showed improvements in social adjustment, family functioning, problem solving, depression, and thoughts about substance abuse, according to Dr. Najavits. "While this is a small sample, an uncontrolled pilot study, the data indicate that, when provided with treatment tailored to their needs, these difficult-to-treat women appear highly responsive and show improvements in both of their diagnoses," she says.

Her treatment design is now undergoing further evaluation in three demonstrations where it is being compared to usual treatment regimens.

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NIH Panel Calls for Expanded Methadone Treatment for Heroin Addiction

By Robert Mathias, *NIDA NOTES* Staff Writer

An expert panel at a National Institutes of Health (NIH) Consensus Development Conference on Effective Medical Treatment of Heroin Addiction has concluded that heroin addiction is a medical disorder that can be effectively treated in methadone treatment programs. The consensus panel strongly recommended expanding access to methadone treatment by eliminating excessive Federal and State regulations and increasing funding for methadone treatment. The conference, which was cosponsored by NIDA, along with the NIH Office of Medical Applications of Research and the NIH Office of Research on Women's Health, was held in Bethesda, Maryland, last November.

Methadone is the medication used most frequently to treat heroin addiction. Outpatient methadone treatment programs administer methadone to reduce patients' cravings for heroin and block its effects, thereby enabling patients to lead productive lives. These programs also may provide counseling, develop vocational skills, and/or provide psychosocial and medical support services to rehabilitate patients. Some patients stay on methadone indefinitely, while others move from methadone to abstinence.

NIH consensus conferences constitute a science forum where a panel of independent nongovernment experts examines the scientific evidence and makes recommendations on an area of medicine. During the course of the conference on treating heroin addiction, the consensus panel, chaired by Dr. Lewis L. Judd of the University of California at San Diego School of Medicine, focused on determining the effectiveness of methadone treatment. After conducting a thorough review of the accumulated data and listening to expert testimony and public debate on the issues, the panel stated unequivocally that addiction to opiate drugs such as heroin is a disease of the brain and a medical disorder that can be effectively treated. Methadone treatment significantly lowers illicit opiate drug use, reduces opiate-related illness and death, reduces crime, and enhances social productivity, the panel concluded.

Despite methadone's effectiveness, less than 20 percent of the estimated 600,000 heroin addicts in the United States are being treated in methadone treatment programs, the panel noted. Many barriers limit the availability of methadone treatment.

These barriers include unnecessary laws administered by a number of Federal agencies and many State and local governments that burden treatment programs with excessive regulatory requirements and duplicative inspections. Some of these regulations restrict treatment programs' ability to tailor methadone doses to the needs of individual patients. Other regulations require physicians to obtain a special Federal registration to use methadone to treat narcotic addiction, thus limiting the number of physicians who are available to treat heroin addiction. Wider use of methadone treatment also is restricted by a shortage of physicians and other health care professionals who are trained to treat heroin addiction, and inadequate funding to provide methadone treatment slots for all those who require them.

The Recommendations

The panel recommended a number of steps to improve access to methadone treatment for all people addicted to heroin and other opiate drugs. The panel's recommendations include the following:

- eliminating unnecessary layers of Federal and State regulation for methadone and similar opiate treatment medications;
- instituting means other than regulation to improve the quality of methadone treatment, such as accreditation of methadone treatment programs;
- improving the training that physicians and other health care professionals receive in the diagnosis and treatment of patients with heroin addiction; and
- increasing funding for methadone treatment, including providing benefits for methadone treatment as part of public and private health insurance programs.

The panel also recommended that additional research be conducted on factors that lead to heroin use; changes in the brain that occur with repeated heroin use and result in addiction; the neurobiological processes of craving; and the differences among individuals who are able to end opiate addiction and those who cannot. In addition, the panel called for a national study to assess the prevalence of heroin addiction in the United States and for rigorous studies of the financial costs of heroin addiction to society and the cost-effectiveness of methadone treatment. **NN**

Study Sheds New Light on the State of Drug Abuse Treatment Nationwide

By Michael D. Mueller and June R. Wyman, *NIDA NOTES* Staff Writers

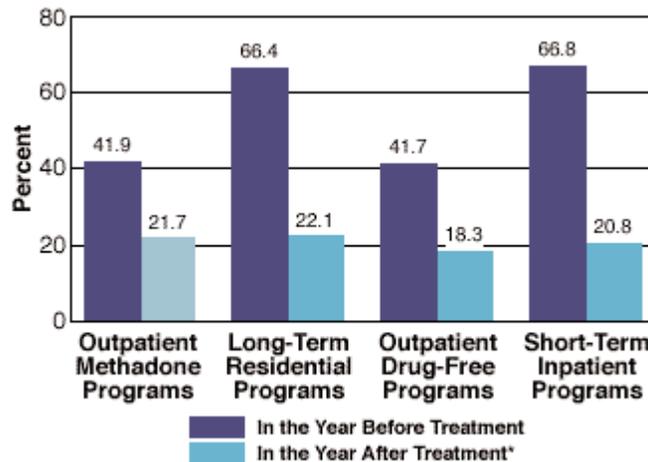
The four most common forms of drug abuse treatment are all effective in reducing drug use. That is the major finding from a NIDA-sponsored nationwide study of drug abuse treatment outcomes. The Drug Abuse Treatment Outcome Study (DATOS) tracked 10,010 drug abusers in nearly 100 treatment programs in 11 cities who entered treatment between 1991 and 1993.

"DATOS is the largest study of drug abuse treatment outcomes since the early 1980s and the most important in the last 10 years in terms of telling us how treatment programs are doing", says Dr. Bennett Fletcher, chief of NIDA's Services Research Branch.

DATOS investigators measured treatment outcomes using a random sample of approximately 3,000 patients. The researchers compared patients weekly and daily drug use for the 12 months before they entered treatment with their weekly and daily drug use 12 months after they stopped treatment. Patients in outpatient methadone treatment who were still in treatment were interviewed approximately 24 months after admission. Other outcomes that the researchers measured included:

- whether patients reported fewer illegal acts, including assault, robbery, burglary, larceny, forgery, and fencing stolen property;
- whether patients were working full time, defined as at least 35 hours per week; and
- whether patients reported fewer attempts or thoughts of suicide, which was used as a marker for depression. The researchers chose that marker because several previous studies had established its validity as an indicator of depression.

Percentage of Patients Reporting Weekly or More Frequent Cocaine Use Before and After Treatment



* Outpatient methadone patients still in treatment were interviewed approximately 24 months after admission. In all four types of treatment programs that the Drug Abuse Treatment Outcome Study examined, the percentage of patients reporting frequent use of cocaine dropped dramatically after treatment.

The four types of programs with the number of programs that DATOS studied in parentheses were outpatient methadone (29), outpatient drug-free (32), long-term residential (21), and short-term inpatient (14). (For descriptions of the program types, see the textbox.) Three of the four types were also studied in DATOS's two predecessors: the Drug Abuse Reporting Program (DARP), which included admissions to treatment from 1969 to 1973, and the Treatment Outcome Prospective Study (TOPS), which covered admissions from 1979 to 1981. The short-term inpatient treatment programs, originally developed to treat alcohol

abuse but admitting increasing numbers of cocaine abusers during the 1990s, were studied in DATOS but not in the two earlier projects.

Highlights From the Study

For the four treatment types, DATOS investigators found reductions almost without exception in the use of all drugs including cocaine, heroin, and marijuana after treatment. (See "Percentages of Patients Reporting Weekly or More Frequent Substance Use Before and After Treatment.") Likewise, after treatment a smaller percentage of patients reported committing illegal acts, working less than full time, and thinking about or attempting suicide. (See "Percentage of Patients Reporting These Behaviors Before and After Treatment.") The data also revealed that:

- Except in outpatient methadone programs, cocaine was the primary drug of abuse, with alcohol running a close second. Cocaine abuse was common even in outpatient methadone treatment programs for heroin addicts. About 42 percent of patients who entered methadone treatment programs also abused cocaine.

Four Common Types of Drug Abuse Treatment

Investigators with the Drug Abuse Treatment Outcome Study (DATOS) studied patients in the four most common kinds of treatment programs:

- Outpatient methadone programs administer the medication methadone to reduce cravings for heroin and block its effects. Counseling, vocational skills development, and case management to help patients access support services are used to gradually stabilize the patients functioning. Some patients stay on methadone for long periods, while others move from methadone to abstinence.
 - Long-term residential programs offer around-the-clock, drug-free treatment in a residential community of counselors and fellow recovering addicts. Patients generally stay in these programs several months or up to a year or more. Some of these programs are referred to as therapeutic communities.
 - Outpatient drug-free programs use a wide range of approaches including problem-solving groups, specialized therapies such as insight-oriented psychotherapy, cognitive-behavioral therapy, and 12-step programs. As with long-term residential treatment programs, patients may stay in these programs for months or longer.
 - Short-term inpatient programs keep patients up to 30 days. Most of these programs focus on medical stabilization, abstinence, and lifestyle changes. Staff members are primarily medical professionals and trained counselors. Once primarily for alcohol abuse treatment, these programs expanded into drug abuse treatment in the 1980s.
- Heroin use had decreased since the 1979 to 1981 period that TOPS studied. Large declines in the abuse of depressants such as barbiturates and tranquilizers had also occurred since TOPS.
 - Short-term inpatient treatment programs yielded significant declines in drug use, even though patients stayed in these programs no more than 30 days. "This is one of our most surprising findings," Dr. Fletcher says. "This treatment mode had a high percentage of patients reporting daily or weekly use of cocaine in the year before treatment and a sharp decline in weekly and daily use after treatment." The percentage of patients reporting illegal acts and thoughts of suicide also declined significantly after treatment in these programs. The researchers are exploring whether continuing involvement in outpatient services and mutual help groups may have contributed to these positive outcomes.
 - In every city studied in DATOS, support services such as medical, legal, financial, psychological, employment, and family services had declined dramatically since TOPS, while the need for those services had increased. (See "DATOS Documents Dramatic Decline in Drug Abuse Treatment Services.")
 - Patients surveyed by DATOS reported that it took them about 7 years after they first used their primary drug to enter treatment. (See "Treatment Histories: The Long View of Addiction.")

The Drug Abuse Treatment Outcome Study found reductions in the use of all drugs including cocaine, heroin, and marijuana after treatment.

New Demographics

Demographic characteristics of patients studied in DATOS had changed since the earlier study. For example, DATOS patients were older and had more years of schooling than TOPS patients, and a greater percentage of them were women.

In DATOS, 39 percent of patients admitted to outpatient methadone programs were women compared to approximately 31 percent in TOPS. Women made up approximately 33 percent of the patients admitted to long-term residential programs, as opposed to 22 percent for TOPS. Outpatient drug-free programs saw little change from TOPS to DATOS, with women accounting for approximately 33 percent of patients in these programs in both studies. In DATOS, about 37 percent of patients admitted to short-term inpatient programs, which were not included in TOPS, were women. The researchers are conducting additional analyses to further explore the characteristics and outcomes for women in DATOS.

Substance Abuse and Psychological Disorders

DATOS researchers looked at co-occurring psychological disorders and dependencies in 7,402 patients in the DATOS programs who were diagnosed as substance dependent. They found that 32.1 percent of those patients were dependent on cocaine alone. Of that 32.1 percent, 59.1 percent were male. Another 26.3 percent of the patients were dependent on both cocaine and alcohol,

When the researchers looked at retention rates, they found big differences within each of the four treatment types and among individual programs.

and, of those, 69.8 percent were male. In addition, 10.6 percent of the patients were dependent on heroin alone, and 64.2 percent of those were male.

The prevalence of co-occurring psychological disorders among the group was high, especially for antisocial personality disorder (APD) and major depression. APD was characterized as a pattern of disregard for the rights of others, irresponsibility, and lack of remorse. Major depression was characterized as either a depressed mood or a loss of interest or pleasure for 2 weeks or more.

The prevalence of those two disorders differed widely among men and women. Approximately 40 percent of the group was diagnosed with APD, and males were twice as likely as females to be diagnosed with the disorder. While 12 percent of the group had experienced a major depression, female patients were twice as likely as male patients to have done so.

Keeping Patients in Treatment

When the researchers looked at retention rates, they found big differences within each of the four treatment types and among individual programs. "We found a lot of diversity in how well they're doing at keeping patients in treatment, and we wanted to know why," says Dr. Dwayne Simpson of Texas Christian University in Fort Worth.

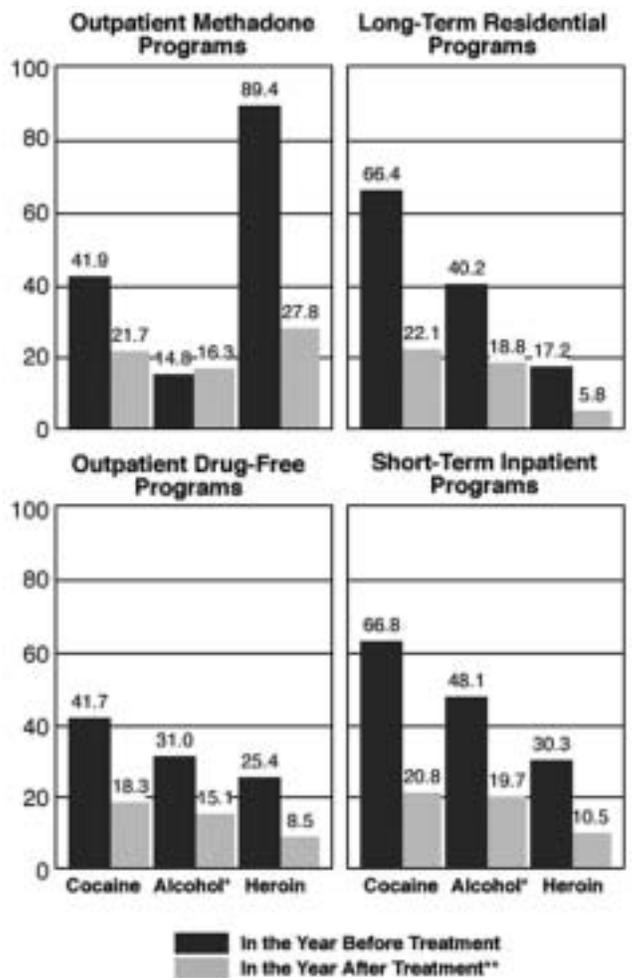
The investigators found that programs with low retention rates tended to have patients with the most problems, particularly antisocial personality disorder, cocaine addiction, or alcohol dependence. In addition, heroin abusers who also abused crack cocaine but not powder cocaine had significantly lower retention rates than other heroin abusers did. "These programs are dealing with some tough people. Programs with the highest concentration of these problem patients naturally tend to have low retention," Dr. Simpson says.

What makes patients stay in treatment? The researchers found that the major predictors were:

- high motivation;
- legal pressure to stay in treatment;

- no prior trouble with the law;
- getting psychological counseling while in treatment; and
- lack of other psychological problems, especially antisocial personality disorder.

Percentage of Patients Reporting Weekly or More Frequent Substance Use Before and After Treatment

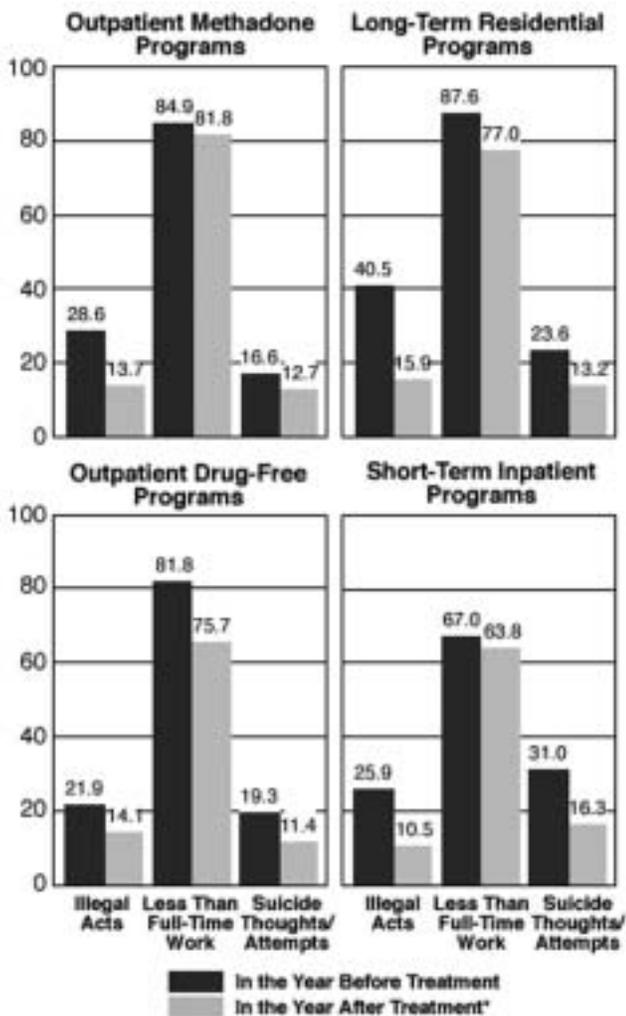


* Weekly or more frequent use with 5 or more drinks at a sitting.

** Outpatient methadone patients still in treatment were interviewed approximately 24 months after admission.

Patients in programs surveyed for DATOS showed a marked reduction in drug use after treatment regardless of the type of treatment program in which they participated. DATOS analyses focused on marijuana use instead of heroin use among patients in short-term inpatient programs and outpatient drug-free programs because the number of patients using heroin in those programs was too small to allow statistical comparisons.

Percentage of Patients Reporting These Behaviors Before and After Treatment



* Outpatient methadone patients still in treatment were interviewed approximately 24 months after admission.

The DATOS data showed reductions after treatment in illegal acts, which included assault, robbery, burglary, larceny, forgery, and fencing; less than full-time employment; and suicidal thoughts and suicide attempts, indicators of depression.

Lessons From DATOS

What were the overall conclusions? "Clearly there were significant changes from before to after treatment in each of the four modalities," says Dr. Fletcher. That finding

raises some interesting questions, he adds. "For example, retention has been our most powerful and consistent predictor of treatment outcomes - yet even people in short-term inpatient treatment for 30 days or less improved significantly." Although DATOS replicated the finding from DARP and TOPS that time in treatment is important, the relationship to retention of other factors such as motivation, psychiatric comorbidity, and treatment process needs to be studied more, he says.

One would also expect worse outcomes from DATOS compared to TOPS because of the steady decline in availability of support services, says Dr. Fletcher. A possible explanation for the better DATOS outcomes is that although support services have decreased, core treatment services have improved. "Core services - basic treatment techniques such as drug abuse counseling, mutual-help groups, and patient participation in devising treatment plans may have improved over the past 10 years. What we're seeing may be a result of this improvement, even though availability and use of noncore support services have declined," Dr. Fletcher says.

The study's encouraging results verify the effectiveness of drug abuse treatment no matter what its form, says NIDA Director Dr. Alan I. Leshner. "The service system has changed dramatically over the last two decades. This study gives us a unique opportunity to understand the effect of those changes and to have an impact on the way treatment is delivered," Dr. Leshner says.

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Treatment Histories: The Long View of Addiction

Drug Abuse Treatment Outcome Study (DATOS) researchers at the University of California at Los Angeles looked at the treatment histories of addicts in treatment to learn more about the life cycle of addiction and how that influences treatment outcomes. For example, when did patients first enter treatment, and how many times had they been in treatment?

Overall, DATOS patients reported that they first entered drug abuse treatment about 7 years after they began using their primary drug. In outpatient methadone programs, patients reported having used heroin for an average of 15 years and having undergone various episodes of treatment for about 7 years. In the three other treatment types—outpatient drug-free, long-term residential, and short-term inpatient—patients had been abusing an average of 11 years and had been in some kind of treatment, often not continuously, for 2 to 3 years.

About one-half of the patients had received treatment prior to entering their current treatment episode, and of those, over one-half had received some prior treatment within the previous year. Patients who reported having had prior treatment also had more severe drug dependence and were more involved in criminal activity compared with those who had not had prior drug abuse treatment.

Despite having more severe histories of drug dependence, patients with prior treatment history who received more support services in addition to basic drug abuse treatment

—such as help with medical, financial, employment, legal, psychological, and family problems—were more likely to be abstinent at one-year follow-up than those who received fewer support services. Similarly, treatment-experienced patients who spent more time in the current treatment episode had better outcomes than those who spent less time in treatment.

These findings suggest that despite repeated treatment attempts and the multiple problems typically associated with a history of severe drug abuse, patients can be successfully treated with a comprehensive treatment approach of sufficient duration, the researchers say. The scientists are currently comparing treatment histories of men and women to see how they differ and to explore the implications of those differences for effective treatment. The researchers conclude that treatment providers can improve treatment of drug abuse by:

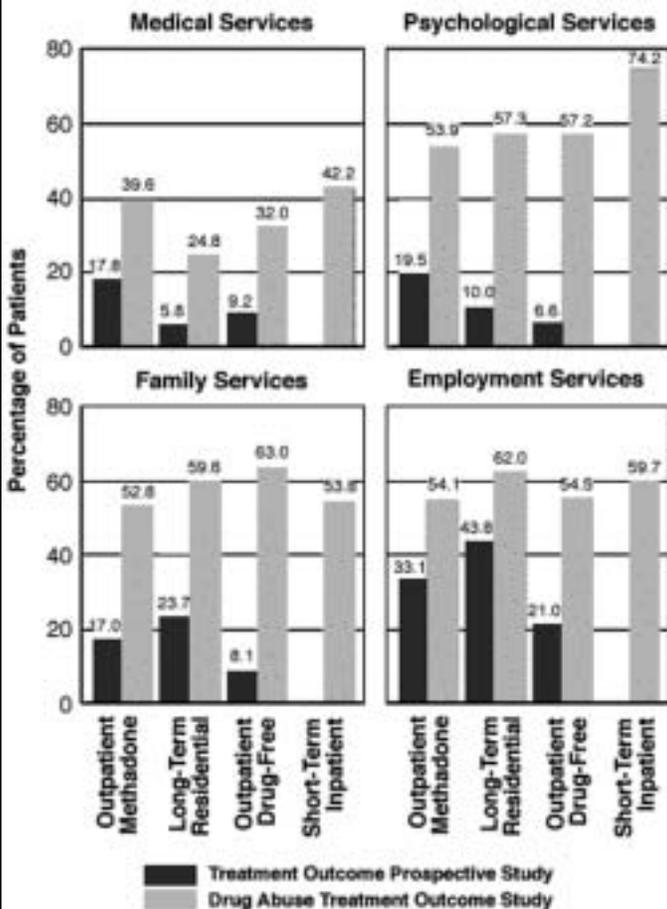
- engaging addicts in treatment as soon as possible;
- offering support services to address the multiple problems of drug abuse patients; and
- coordinating treatment episodes.

Source

- Anglin, M.D.; Hser, Y.; and Grella, C.E. Drug addiction and treatment careers among clients in DATOS. *Psychology of Addictive Behavior*, in press. **NN**

DATOS Documents Dramatic Decline In Drug Abuse Treatment Services

Patients in Treatment Who Needed But Did Not Receive Support Services: TOPS vs. DATOS



* Short-term inpatient programs were not studied under TOPS.

Patients in the drug abuse treatment programs studied in DATOS reported unmet needs for additional support services much more often than did patients surveyed in TOPS, the earlier study, which covered treatment admissions from 1979 to 1981.

Drug Abuse Treatment Outcome Study (DATOS) researchers report a widening gap over the last decade between patients' needs for support services that go beyond basic treatment techniques such as drug abuse counseling and the availability of those services. Such support services address medical, psychological, family, legal, vocational, and financial problems with which many drug abusers need help to stay in treatment, reduce substance abuse, and improve other areas of social functioning.

The investigators compared the type and number of both core drug abuse treatment services and support services with those that had been delivered a little over a decade before with the Treatment Outcome Prospective Study (TOPS). "What we found was alarming. In every problem area studied, the type and number of support services had decreased from TOPS to DATOS, while the need for those services had increased," says Dr. Bennett Fletcher, chief of NIDA's Services Research Branch.

Dr. Rose Etheridge and her colleagues at the National Development and Research Institutes in Raleigh, North Carolina found that more than half of DATOS patients in all four types of treatment-outpatient methadone, long-term residential, outpatient drug-free, and short-term inpatient - did not report receiving many services that they said they needed.

Some 65.3 percent of DATOS patients in outpatient methadone programs reported that they did not receive any support services during the critical first three months of treatment compared to 49.5 percent in TOPS. In outpatient drug-free programs, 60.2 percent of DATOS patients said that they did not receive such services compared to 18.2 percent of TOPS patients.

Few gender differences were found in patient reports of services received and unmet service needs after three months in treatment. Only small gender differences were found in unmet needs in DATOS compared to TOPS.

Source

- Etheridge, R.M.; Craddock, S.G.; Dunteman, G.H.; and Hubbard, R.L. Treatment services in two national studies of community-based drug abuse treatment programs. *Journal of Substance Abuse* 7:9-26, 1995.

■ ■

National Study Offers Strong Evidence of the Effectiveness of Drug Abuse Treatment

NIDA Director Dr. Alan I. Leshner

A newly released nationwide study shows impressive reductions in drug use for patients in the four common types of drug abuse treatment. This good news comes from the NIDA-supported Drug Abuse Treatment Outcome Study (DATOS)—a major research effort that tracked more than 10,000 patients in almost 100 programs in 11 cities around the Nation over 3 years. Building on two earlier nationwide studies of treatment outcomes, DATOS investigators have amassed a wealth of information on drug abuse treatment outcomes, psychological disorders, retention rates, and treatment histories of drug abusers. The study also provides new information on changes in availability of drug abuse treatment services—ranging from basic drug abuse counseling to medical, legal, employment, and financial help—over the last two decades.

DATOS overwhelmingly confirms the effectiveness of drug abuse treatment. Although the two earlier studies and many smaller-scale studies have documented this effectiveness, DATOS proves it with nationwide findings for the 1990s. (See "Study Sheds New Light on the State of Drug Abuse Treatment Nationwide.") Among the patients that DATOS studied, drug use dropped significantly from the 12 months before treatment to 12 months after treatment began. This was true for all four types of treatment studied: outpatient methadone, outpatient drug-free, long-term residential, and short-term inpatient. Treatment also led to significant improvements in other aspects of patients' lives such as reduced involvement in illegal acts.

DATOS is one of the few national longitudinal studies to collect data on psychological disorders among drug abusers in treatment. The study also provides invaluable insight into critical differences between men and women entering drug abuse treatment. Knowing the gender-specific problems of addicts entering treatment can help providers tailor treatment to patients' specific needs.



The Drug Abuse Treatment Outcome Study overwhelmingly confirms the effectiveness of drug abuse treatment with new nationwide findings.

DATOS also provides a wealth of information on the demographic characteristics and treatment histories of addicts in treatment. (See "Treatment Histories: The Long View of Addiction.") As more data are analyzed, researchers will be able to link patients' treatment outcomes to their backgrounds, gender, treatment histories, psychological disorders, and the specific services they have or have not received. This knowledge will enable us to refine and strengthen treatment by helping service providers determine what treatments work best for what kinds of patients.

Although much of the news from DATOS is good, there is also cause for concern. The study identified an alarming drop over time in the provision of services such as medical, legal, employment, and financial help. This decline is of special concern, since drug abusers often need help in one or more

of these areas to get into and stay in treatment. Since NIDA's last national study of treatment outcomes, conducted from 1979 to 1981, the provision of these services has declined strikingly while the need for them has increased. From 1991 to 1993, during the time DATOS researchers were collecting data, the typical length of stay in short-term inpatient treatment dropped from 28 days to 14 or fewer days as insurers reduced coverage for addiction treatment. These changes did not go unnoticed by patients. More than half of DATOS participants in the four kinds of treatment programs surveyed did not report receiving support services that they said they needed. And, nearly 75 percent of patients in short-term inpatient programs reported not getting the psychological help they needed. (See "DATOS Documents Dramatic Decline in Drug Abuse Treatment Services.")

The reality is that we now have a treatment system that faces major resource constraints. As drug abuse treatment comes increasingly under managed care and resources are

more tightly controlled, we must stay focused on the scientific facts about addiction and how to treat it adequately. Managed care providers must make tough decisions in allocating their resources, and DATOS can provide the hard scientific data they need to guide those decisions.

Given the wealth of findings coming from this study, our challenge is to communicate this information to health care organizations, managed care companies, and public policymakers. We have a new mechanism in place to do that. Disseminating research findings is a primary goal of

NIDA's new Treatment Initiative, as described in the last issue of *NIDA NOTES*. (See "NIDA Initiative Will Stimulate Improvements in Drug Abuse Treatment," and "NIDA Launches Drug Abuse Treatment Initiative," V12-4, July/August 1997.) The DATOS results together with the Treatment Initiative can help us bridge the gap between public perceptions of drug addiction and what science has again shown—that drug abuse and addiction can be treated successfully with science-based methods, adequate treatment, and vigilant followup. **NN**

Targeting Drug Abuse Treatment Programs to the Homeless

By Neil Swan, *NIDA NOTES* Staff Writer



NIDA-funded research projects are examining treatment options for homeless substance abusers. Patients in a Birmingham, Alabama program are offered housing and taught skills such as carpentry and painting as long as they stay drug free.

Perhaps no group in society is more elusive, more difficult to help than the Nation's homeless. They are often loners who tenaciously avoid contact with others and often shun offers of assistance. They are often in dire need of food, shelter, health care, and other basic necessities. Research shows many are also mentally ill, usually with serious psychiatric disorders. Among these homeless people, who some estimate may number 600,000 or more nationwide, substance abuse is common.

Attempts to treat these homeless substance abusers with multiple problems have not proven effective due to difficulties in recruiting them for treatment. For those who do enter treatment, dropout rates are high. But two separate NIDA-funded treatment research projects, in New York City and Birmingham, Alabama, are testing innovative therapy approaches that are showing promising treatment outcomes. The programs counter patient recruitment and retention problems by coordinating efforts with existing homeless shelters and social service agencies. Both projects treat substance abuse in novel ways. They seek to move patients from highly structured and focused interventions to more flexible treatment regimens as these patients progress toward self-sufficiency by living with peers, paying rent, and working.

The New York City project, provides residential treatment tailored to meet the diverse needs of homeless substance abusers who are also mentally ill. The Birmingham project, includes "contingency management" in which patients who remain drug free gain access to housing and work therapy. **NN**

Peer Community Helps Homeless Drug Abusers With Mental Illnesses Reduce Drug Use

By Neil Swan, NIDA NOTES Staff Writer

"I made good friends here. I call them family . . . Even the staff, they are my family. They gave me suggestions, ideas, looking to my future. They helped me. . . I had 2 years of college, but I didn't get anything out of it. I was using [crack]. . . I see myself with a future now. . . Now I want to work for my money. I plan to get my children back, and I am seeking housing for me and my children."

- Sarah, a graduate of a program in New York City for homeless, mentally ill substance abusers

Researchers at the Center for Therapeutic Community Research (CTCR) in New York City, one of NIDA's major multidisciplinary research centers, are studying a treatment program they devised to meet the complex psychiatric and substance abuse needs of homeless substance abusers who are also mentally ill. They have designed a "modified therapeutic community (TC)" that provides 24-hour-a-day supervised residential treatment for 12 months or more followed by less intense aftercare in which patients live alone or together in apartments and hold down jobs.

Patients are recruited into the program by counselors at New York City homeless shelters and psychiatric facilities. Staff members, some of them former homeless substance abusers themselves, help make the program attractive to the homeless. The NIDA-funded treatment research was conducted by the Center at the National Development and Research Institutes. Led by CTCR director Dr. George De Leon, the research has shown that the modified TC program can be effective in treating this elusive population that has "fallen through the cracks" in traditional treatment approaches. Patients substantially reduce drug use and criminal behavior following treatment and also find and keep jobs more frequently than before treatment.

The original TC approach was developed to treat serious substance abusers in a residential program by changing their behavior and thinking. Support of the treatment

This program for homeless, mentally ill substance abusers can be effective in treating an elusive population that has "fallen through the cracks" in traditional treatment approaches.

program members—peers and counselors—is a key ingredient of TCs, which have been enhanced over the years with additional services for vocational, medical, family, and other needs. Today's TC has more participation from mental health, medical, and education pro-

fessionals who serve along with TC paraprofessionals who are trained recovered addicts.

The TC approach, according to Dr. De Leon and his colleagues, views substance abuse as a disorder of the whole person. Thus the approach provides a combination of social and psychological therapy that fosters change in patients' behavior, attitudes, feelings, and values. Individuals are motivated to change through their interaction with others, including their peers from the streets. The New York City research is built on a concept of "community as method," which uses the treatment community itself and its activities, relationships, and expectations to enable patients to learn about and change themselves.

Dr. Stanley Sacks, CTCR's deputy director, explains that the resident community, which usually consists of 12 to 20 patients, provides a structured daily regimen with morning and evening community meetings, seminars, classes, conflict-resolution therapy sessions, and a peer work structure in which community members maintain the facility and prepare their meals. The residents progress toward reentry into society by moving first through a transitional program in which they share apartments with other patients. Mutual support and community ties are continued while patients advance toward entering the job market. Some are employed in clerical or maintenance positions; others eventually become peer counselors in similar recovery programs. After 6 to 12 months of transitional apartment living - 18 to 24 months after entering the residential program - patients advance to independent living while maintaining kinship ties with peers and holding jobs.

The fundamental needs of the patients were extensive, combining psychiatric, substance abuse, medical, and social problems that were acute and intricately intertwined.

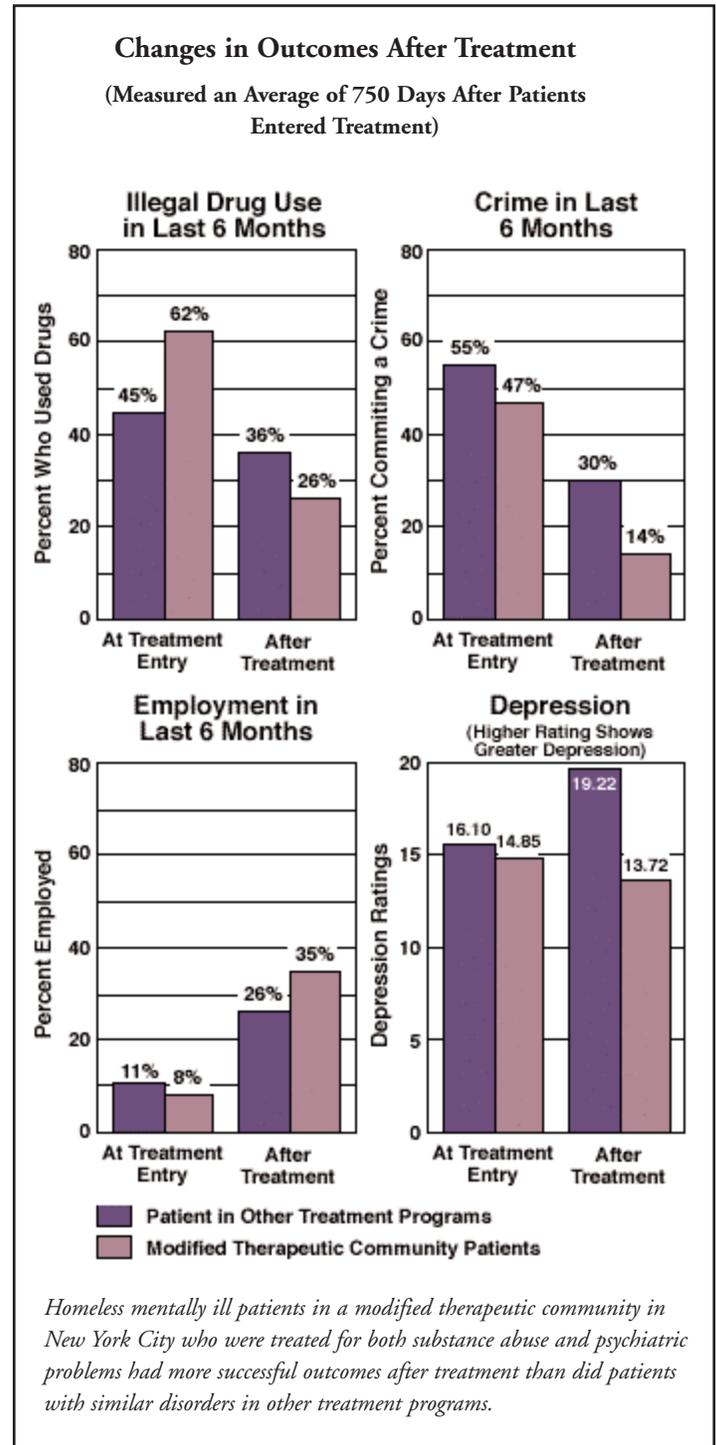
The CTCR study profiled 342 homeless patients as they entered the modified TC program. Interviews by CTCR researchers showed that the fundamental needs of the patients were extensive, combining psychiatric, substance abuse, medical, and social problems that were acute and intricately intertwined. The patients interviewed were three-quarters male and 70 percent African-American, with a median age of 35. The researchers found that 99 percent reported illegal drug use some time in their lives; 24 percent reported injecting drugs. Half reported crack or cocaine as their primary drug of abuse; 22 percent cited alcohol and 16 percent identified marijuana as their secondary substance of abuse. Some 84 percent of the patients had not had a job in the past year. Four in 10 said they had had difficulty throughout their lives in making and keeping friends. Virtually all, 99 percent, of the patients reported past criminal activity, and 81 percent said they had broken the law in the past year. Three-quarters of the patients said they had been tested for infection with HIV, the AIDS virus, and 10 percent reported positive HIV test results.

Using a standardized diagnostic test, the researchers also found that 60 percent of their patients had one or more serious mental illnesses—38 percent were diagnosed with major depression, 34 percent with schizophrenia, and 13 percent with mania. When other mental disorders such as posttraumatic stress disorder and phobia were included, 82 percent of the patients had diagnoses of serious mental illness.

The modified TC targets treatment to meet these multidimensional needs. Compared to standard TC programs, treatment interventions are more individualized, more flexible, and less intense, explains Dr. Sacks. However, the program remains grounded in peer interactions and the "community as method" concept to foster change, he says.

Even in the face of the homeless patients' severe and accumulated problems, the modifications to the TC model are proving effective, initial treatment outcome data indicate. Patients in modified TCs had more successful outcomes at followup, an average of 750 days after entering treatment, than did other New York patients with similar diagnoses who were enrolled in more conventional treatment programs. Those in modified TC treatment reported less

illegal drug use and less criminal activity and showed greater improvement on tests to evaluate depression compared with the conventional treatment patients. In addition, those in modified TC showed important gains in employment levels compared with their pretreatment levels. (See "Changes in Outcomes After Treatment," at bottom of page.)



Aftercare is critical for these patients as they progress toward independent living, says Dr. De Leon. Mental health and medical needs are the most pressing, he adds. Patients who enter treatment with a long history of severe drug abuse—10 years or more— and psychiatric problems require more time than do others in the program, he says. But it may be possible to shorten the time in the residential setting with improved aftercare services, he adds.

Currently, NIDA is supporting a CTCR study to examine the cost-effectiveness of the modified TC program. This study is evaluating program costs against benefits to society measured in taxpayer savings through reduced crime and social services expenditures and increased tax revenues as patients become productive wage-earners. Also with NIDA funding, CTCR is evaluating a modified TC for mentally ill substance abusers in the San Carlos Correctional Facility in Pueblo, Colorado.

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Access to Housing and Job Training Helps Recovering Homeless People Stay Drug Free

By Neil Swan, NIDA NOTES Staff Writer

"I came to the city, and my first day here I spent all my money - \$800 - on drugs. For the first time in my life I was homeless, and it set into me that I was addicted. . . . I entered treatment, and I think that without drug screening early on, I would never have stayed clean. Housing was important, too. In a shelter or on the streets, being around using people makes it almost impossible to recover. . . . I'm clean today, two years down the road. I work in construction; I made \$40,000 last year. I'm making restitution for my child support. I fly my son down for visits during the summers."

- Mr. C., who successfully completed a treatment program in Birmingham, Alabama with access to housing and work therapy

Therapy targeting homeless crack and alcohol abusers reduces substance abuse more if it offers patients housing and jobs, NIDA-funded research has shown. A key component is a requirement that participants stay drug free to remain in the housing and enter work therapy, according to the study's researchers at the University of Alabama at Birmingham.

This therapeutic approach, in which rules and consequences are applied to help people change their behavior, is called contingency management. In the Birmingham program, access to housing and employment is contingent on following the rules, which homeless participants soon learn: stay clean of drugs and alcohol, and you can live in a furnished apartment and enter work therapy. Test positive for drugs or alcohol and you go back into a shelter and lose your job until you are drug free.

The approach works. The Birmingham researchers have demonstrated that participants in the contingency management program remained abstinent from drugs substantially longer than patients who did not receive contingency-based housing and work therapy. "The contingencies for reinforcements of housing and a job are powerful motivators," says Dr. Jesse B. Milby, principal investigator for the project.

Program participants were either homeless or at risk of becoming so. Three-quarters of the patients were male, and 83 percent were African American. Average age was 38 years; average time spent in school was 12.5 years.



Patients in the Birmingham Alabama treatment program who participate in the work therapy program develop a sense of pride and kinship while learning job skills such as carpentry and painting.

Some 79 percent met criteria for one or more mental disorders - 56 percent for mood disorders, 39 percent for anxiety disorders, 6 percent for adjustment disorders, 4 percent for psychotic or organic mental disorders, and 4 percent for other mental disorders. The drug that participants said they used most frequently was cocaine followed by alcohol then marijuana.

In the study, participants were placed for 2 months either in existing local substance abuse treatment programs or an intensive day treatment program that included contingency management. The conventional treatment program consisted of weekly, 12-step-oriented group meetings and individual counseling sessions.

The intensive day treatment required program attendance for 5 1/2 hours every weekday, including group and individual counseling sessions and participant involvement in goal-setting exercises. Intensive day treatment patients also received transportation, lunch, and individual counseling. Patients who completed day treatment were then eligible for the contingency management component - housing and 4 months of work therapy refurbishing abandoned or dilapidated houses as long as they stayed drug-free. The renovated dwellings became housing for participants who met contingency requirements. So far, patient-workers have renovated six houses and have worked on four small apartment buildings now used as drug-free housing.

In the work program, patients learned job skills like carpentry and painting. They worked for "Bad Boy Builders," operated by a Birmingham contractor, and received minimum wages, which they used to pay modest rent for their own housing in dwellings that were previously refurbished by other program enrollees. The contractor provided tools,

materials, insurance, and on-the-job training. Job references were provided for successful patients seeking to move on to other jobs.

Patients moved into the housing after four successive "clean" urine tests. Those who tested positive for drug use were immediately evicted from their apartments and taken to a local shelter to stay during the eviction. Following two successive clean drug tests, these participants

were readmitted to their apartments. Most wanted to move back, and most qualified with clean tests, Dr. Milby says. After completion of the 4-month work therapy, treatment graduates were permitted to remain in the program-provided housing. Some program graduates continue to live in this housing, paying rent.

In the work therapy phase, the program seeks to establish a sense of pride, kinship, and unity among patients. One way the program builds this sense of community is by membership in Club Birmingham. The club holds social activities and distributes identification cards and tee shirts with the club logo.

"We want to provide models of social and recreational activities that are not related to substance abuse," says Dr. Milby. "When they have been homeless and using cocaine and alcohol for a long time, they forget that there are other ways to have fun. We give them a chance to enjoy themselves in drug-free settings like cookouts and fishing parties."

Investigators found that participants in treatment with contingencies were more likely than those in conventional treatment to test clean of drugs, move into stable housing, and be employed regularly following treatment. Those receiving the 4 months of contingency management had 18 percent fewer positive cocaine tests than did conventional care patients after 6 months. That study demonstrated that a multicomponent treatment that addresses homelessness, employment problems, and substance abuse may be the key to successful therapy, Dr. Milby says. However, he notes that participants in the day treatment group spent four times longer in counseling sessions, which is an important variable in addition to contingencies. "We questioned whether the intensive day treatment with contingencies was necessary or whether intensive day treatment alone was sufficient for best results."

A second study was designed to answer this question. In this study, currently under way, all participants are exposed to the intensive day treatment, but only half of the participants receive the abstinence-contingent housing

Patients in the study who tested positive for drug use were immediately evicted from the program housing and taken to a local shelter to stay during the eviction. Following two successive clean drug tests, they were readmitted.

and work therapy. A vocational counselor assists participants in developing job goals. Also, participants are allowed to enter program-provided housing as soon as they are drug-free for four successive tests. As a result, most participants move into the housing during day treatment. Once they complete day treatment, they move into work therapy and begin paying for housing. To help avoid relapse, aftercare therapy follows day treatment.

In this second study, several refinements have been made to the treatment regimen. Each week, patients define specific goals on issues such as addiction, housing, jobs, legal problems, psychiatric concerns, and family relations. "Patients review their own performance in meeting goals, and they are rated aloud by their peers and counselors," says Dr. Cecelia Lee McNamara, project coordinator. "They build self-esteem with a record of accomplishments on their goal sheets."

Following the 4 months of work therapy, clients in day treatment with the contingency management component were drug free an average of twice as many weeks as participants who received only day treatment. The two groups showed equally improved outcomes for days of homelessness and days of employment.

From the second study, it appears that the abstinence contingency works most powerfully on substance abuse, says Dr. Milby. This study also shows that contingency management with day treatment may also reduce the risk of transmission of HIV, the virus that causes AIDS, according to Dr. Joseph Schumacher, another investigator.

Because of the increased costs of providing contingency management, Dr. Milby and his team next plan to study the cost-effectiveness of the enhanced day treatment when used in combination with contingency management.

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NIDA Launches Drug Abuse Treatment Initiative

By Robert Mathias, NIDA NOTES Staff Writer

Several years ago, a NIDA-supported researcher in Vermont discovered that a new behavioral treatment could reduce cocaine abuse among mostly white rural patients. Later, when NIDA intramural and extramural researchers in Baltimore tested the same treatment with inner-city cocaine and heroin abusers, they found that it reduced their cocaine abuse, too. These researchers have shown that this behavioral treatment can reduce cocaine abuse among a variety of patients in controlled clinical research studies. However, they still have more to learn. For example, how well will the treatment work in a resource-starved neighborhood clinic? What training will treatment counselors need to use the new therapy effectively? Will the new treatment be cost-effective?

How to translate promising drug abuse treatments from research into practice is one of the many critical issues that will be addressed by a major Treatment Initiative NIDA has launched to improve the quality of drug abuse treatment.

The Initiative has both a research and a communications thrust. The research thrust will stimulate additional work to improve current treatments and to develop new treatments and transfer them to community-based drug abuse treatment clinics. The communications thrust will increase the exchange of useful information about drug addiction and its treatment among the research and treatment communities and the general public.

"We now have a variety of effective addiction treatments as a result of our research," says NIDA Director Dr. Alan I. Leshner. Both behavioral and pharmacological treatments have been shown to reduce drug abuse, crime and delinquency, and the spread of HIV/AIDS and other infectious diseases that are associated with drug abuse, he points out. "By spurring additional drug abuse treatment research and speeding the evaluation and application of research-tested treatments in the real world, NIDA's Treatment Initiative can have a significant impact on the Nation's public health," he says.

Under the research prong of the Initiative, NIDA will hold workshops to assess the current body of scientific

The Treatment Initiative will spur additional drug abuse treatment research and speed the evaluation and application of research-tested treatments in the real world.

knowledge about behavioral therapies, treatment medications, HIV/AIDS risk behaviors, and comprehensive treatment services. The Institute also plans to solicit and support new research to meet needs identified in all of these areas throughout the course of the Initiative.

Advancing the role of behavioral therapies in drug abuse treatment is a priority of the Treatment

Initiative, says Dr. Lisa Onken of NIDA's Division of Clinical and Services Research (DCSR). Dr. Onken is coordinating the Initiative with Dr. Stephen Zukin, who heads the Division. This fall, DCSR is holding workshops on translating the findings of basic behavioral science research into innovative behavioral therapies and on transferring clinically tested behavioral therapies to the community treatment setting. Two other workshops are examining adolescent treatment issues. One is focusing on the development of more effective treatment approaches to deal with the special needs of adolescents. The other workshop is addressing how to develop early treatment strategies for adolescents and preadolescents who are beginning to abuse drugs.

Advancing health services research also will be an important part of the Initiative. This year, the Initiative is holding health services workshops on:

- factors that influence patients' readiness for treatment and motivation to change. This workshop also is exploring alternative approaches to drug abuse treatment for patients unable or unwilling to seek help in traditional treatment programs.
- drug abuse treatment for special populations such as racial and ethnic minorities, the homeless, persons with disabilities, and pregnant women. Unique treatment needs, potential barriers to treatment, and culturally appropriate treatment models to set research priorities to improve treatment for these populations are among the issues on the agenda.
- integrating medical and mental health services and drug abuse treatment. This workshop aims to promote cross-system health services research by increasing

communication and interaction between medical health services researchers and drug abuse treatment researchers.

- financing drug abuse treatment and services. An expert panel is convening at this workshop to develop research recommendations to address both the immediate and long-term funding needs of providers of treatment resources.

Other Treatment Initiative research workshops on this year's agenda are designed to:

- evaluate the validity and reliability of instruments that researchers are currently using to assess whether drug abuse treatment reduces AIDS risk behaviors; and
- look at ways to improve and expand the use of the heroin treatment medication naltrexone.

Under the communications thrust of the Initiative, NIDA will hold a major drug abuse treatment conference in April 1998. The conference will highlight the principles of effective drug abuse treatment; detail pharmacological and behavioral treatments that have been shown to be effective; and examine the state of current research on special populations. The audience for the conference will include treatment researchers, treatment providers and practition-

ers, representatives from State drug abuse agencies and managed care organizations, and public policymakers. "We want to invite anyone who has an impact on treatment," said Dr. G. Alan Marlatt of the University of Washington in Seattle at a recent meeting of NIDA's National Advisory Council on Drug Abuse. Dr. Marlatt serves on a Council subcommittee that is helping NIDA plan the treatment conference and focus the Treatment Initiative.

In addition to the treatment conference, NIDA plans a host of other communications activities for the Initiative. Several work-shops will identify and disseminate research-based behavioral therapies.

Additional conferences will update the drug abuse treatment community on the treatment of cocaine addiction, heroin treatment medications, and other effective drug abuse treatment and HIV prevention approaches. Treatment research symposia at major national meetings will inform professionals in related fields about drug abuse treatment research findings.

NIDA NOTES will provide further information about the Treatment Initiative's conferences, symposia, and work-shops as details become available. **NN**

NIDA Initiative Will Stimulate Improvements In Drug Abuse Treatment

NIDA Director Dr. Alan I. Leshner

Over the years, researchers have amassed an impressive amount of scientific knowledge about the treatment of drug abuse and addiction. This research has clearly shown us that drug abuse treatment can reduce drug use, drug-related criminal behavior, and the health and social costs of drug abuse and addiction.

In addition, NIDA has funded the development of several new behavioral treatments for cocaine abuse that have shown good success in clinical trials. Family therapies for adolescents, contingency management approaches, and cognitive-behavioral therapies are now ready for use in treatment programs. In addition, clinics around the Nation are using medications such as methadone and the NIDA-developed LAAM (leva-alpha-acetyl-methadol) in combination with behavioral treatments to treat heroin addicts successfully. Developing an effective medication to treat cocaine addiction continues to be a major NIDA priority, and we have a number of promising compounds in our medications development pipeline.

Despite advances such as these, we need to do more to reduce the ravages of drug abuse and addiction. Therefore, NIDA has launched a major Treatment Initiative to further improve the effectiveness of drug abuse treatment. This Institute-wide effort is being coordinated by NIDA's Division of Clinical and Services Research. A special subcommittee of NIDA's National Advisory Council on Drug Abuse is helping us focus the Initiative's priorities. Over the next few years, the Treatment Initiative will increase NIDA's treatment research and dramatically expand the dissemination of information about research-proven drug abuse treatments.

To increase the usefulness of NIDA's existing base of treatment knowledge, our comprehensive Initiative will sponsor a series of research workshops to bring together experts in different areas of treatment. These experts will evaluate existing addiction treatments and determine



NIDA's comprehensive Treatment Initiative will be the catalyst for more effective drug abuse treatments.

which treatments work best and how they work. They also will recommend additional research to develop new and more potent behavioral and pharmacological therapies. Ultimately, these efforts should expand the treatment options available to practitioners and enable them to select the right combination for their patients.

The NIDA National Advisory Council Subcommittee on the Treatment Initiative has urged increased emphasis on the development of new behavioral therapies, the transfer of effective behavioral therapies into practice, and the development of new pharmacological and behavioral treatments for methamphetamine abuse. The Initiative will address the first two of these priorities with a series of workshops on practical issues involved in behavioral therapies development and application.

And, to meet the challenge of methamphetamine abuse, NIDA has called for expanded research to develop medications to treat abuse of psychomotor stimulants other than cocaine, particularly methamphetamine.

The Treatment Initiative also will expand health services research to get a clearer picture of how the organization, management, and financing of drug abuse treatment affect its accessibility, availability, costs, and results. This research will enable us to evaluate and further improve the effectiveness and cost-effectiveness of drug abuse treatment in the real world. In turn, these data will help us to respond successfully to ongoing changes in the delivery and financing of health care. We have already begun this process by issuing a new Request for Applications to encourage additional health services research in these areas.

The Initiative will launch extensive information dissemination activities to address directly what I consider to be the greatest barrier to improving drug abuse treatment today—a general disbelief in the effectiveness of drug abuse treatment. I believe that this "great disconnect" between public perceptions and what science has shown—

that drug abuse is clearly treatable—stems from general ignorance about these findings. Simply put, the public lacks knowledge about the biological and behavioral changes wrought by drug abuse and addiction and the success of treatment in addressing these changes. This lack of knowledge undermines our ability to treat this chronic, relapsing disease effectively. It also erodes support for the research we need to further improve drug abuse treatment.

To bridge this disconnect, the Treatment Initiative will spread the word that we have effective drug abuse treatments that work well for many people. In addition, the conferences, research symposia, and workshops that the Initiative will sponsor over the next few years will greatly increase the flow of scientific information about drug addiction and treatment issues among researchers, policymakers, the treatment community, and the general public. For example, all of these constituencies will be invited to a major treatment conference next April where treatment researchers will spotlight what we know about addiction

and models of successful addiction treatment. Taken together, these coordinated activities will increase understanding of drug abuse treatment research. These activities will also demonstrate to the public, policymakers, and public and private agencies that funding drug abuse research and treatment is well worth the money. (For full details of activities that are being planned for the Treatment Initiative, see "NIDA Launches Drug Abuse Treatment Initiative.")

The news about drug abuse treatment is good news. Many studies have shown the effectiveness of drug abuse treatment. And we have the knowledge and the tools to develop drug abuse treatments that will work even better tomorrow. I firmly believe that NIDA's comprehensive Treatment Initiative will be the catalyst for more effective drug abuse treatments that will substantially alleviate the heavy individual, family, and societal costs and consequences of this terrible disease. **NN**

NIDA Sends Clinical Toolbox to 12,000 Drug Abuse Treatment Providers

By Josephine Thomas, *NIDA NOTES* Contributing Writer

NIDA has mailed the new "Clinical Toolbox: Science-Based Materials For Drug Abuse Treatment Providers" to 12,000 treatment providers across the Nation. The Toolbox was developed to respond to the need expressed by treatment professionals for research materials that document the best treatment practices.

"The Toolbox is one of NIDA's most important responses to our mandate to disseminate state-of-the-art research information about drug addiction and its treatment," says NIDA Director Dr. Alan I. Leshner. "It provides treatment professionals with a wealth of materials on new and effective approaches to helping individuals with drug-related problems."

The Toolbox materials are housed and mailed in a box similar to a magazine file, which is designed to accommodate future NIDA publications on effective drug abuse treatment approaches as they are published. The materials include a variety of publications based on NIDA-supported research, including the following:

- Principles of Drug Addiction Treatment: A Research-Based Guide, one of NIDA's most popular publications. The 54-page booklet presents the 13 principles of effective drug abuse treatment, answers frequently asked questions, describes categories of treatment programs, and offers examples of scientifically validated approaches to treating drug addiction.
- The first three in a series of drug abuse therapy manuals, which offer information to help treatment practitioners provide consistent comprehensive and effective care. The therapies in the three manuals reflect the current state of knowledge in the field of cocaine addiction treatment. The manuals are: A Cognitive-Behavioral Approach: Treating Cocaine Addiction; A Community Reinforcement Plus Vouchers Approach: Treating Cocaine Addiction; and An Individual Drug Counseling Approach To Treat Cocaine Addiction: The Collaborative Cocaine Treatment Study Model. Future manuals will relate to other areas of drug abuse and treatment, including family treatment to address the needs of adolescents with drug abuse problems.
- Six NIDA Research Reports, each of which summarizes the findings of researchers with respect to the scope, effects, treatment, and prevention of abuse of a

particular drug or class of drugs: anabolic steroids, cocaine, methamphetamine, nicotine, inhalants, and heroin.

- Approaches To Drug Abuse Counseling, a book that provides detailed descriptions of 12 drug abuse counseling models currently in use in the United States. Each of these approaches has made substantive contributions to the field, and many serve as models for other programs that have been launched successfully or are in development.
- A Commonly Abused Drugs chart, a laminated reference card that provides information about most major drugs of abuse, their commercial and street names, their short- and long-term effects, their modes of administration, and their Drug Enforcement Administration controlled substances schedules.
- NIDA's Publications Catalog, which lists all available NIDA publications, posters, curricula, audio/video materials, and other products and provides information on how to order them.

To Receive This Resource

The Clinical Toolbox (NCADI publication number CLNBOX) is available from the National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD 20847, phone 800-729-6686; fax 301-294-5516; TTD 800-487-4889; e-mail info@health.org. The Toolbox is available for a small shipping fee. Many of the publications included in the Toolbox also are available online at NIDA's home page at www.drugabuse.gov. **NN**



A wide variety of science-based drug abuse treatment information is included in NIDA's Clinical Toolbox.

following areas: medical symptoms, employment and self-support, drug use, alcohol use, legal status, family and social relationships, and psychiatric symptoms.

Randomly selected matched-services patients received focused services in the areas of employment, family relations, or psychiatric problems, depending on their needs. These problem areas were targeted because studies had shown them to be most important in predicting poor treatment outcome. The treatment providers gave these matched patients a minimum of three individual therapy sessions from a psychiatrist, psychologist, or social worker, for each identified problem. For example, matched patients with a psychiatric problem received at least three targeted individual therapy sessions from a psychiatrist or psychologist. Standard patients were also interviewed with the ASI. The information was provided to the treatment programs, and the programs were asked to treat them "in the usual manner."

Both matched- and standard-treatment patients were monitored with weekly phone calls and were evaluated again with the ASI interview 6 months after discharge. The results showed that matched-treatment patients stayed in treatment longer, were more likely to complete treatment, and had better 6-month outcomes than the standard-care patients treated in the same programs. The standard-care group showed significant improvements between admission and 6-month followup in drug use, alcohol use, family relations, and psychiatric problems, but failed to show improvements in medical status and showed significantly worsened status in employment. The

matched group showed statistically significant improvement in all ASI problem areas.

The researchers caution against generalizing their findings to other groups. The study patients were referred by an employee assistance program and thus probably differed from other insured groups in the amount of pressure they were under to enter treatment, as well as in aspects of their backgrounds, the researchers note.

The matching strategy was clinically and administratively practical and attractive to patients, the researchers say. The results indicate that, despite obstacles to matching patients to programs, strategies can be designed to target services effectively within programs.

"In the real world of addiction treatment, providers can find ways to best utilize treatment resources," says Dr. McLellan. "Each patient's unique treatment needs can be identified easily and reliably at the time of treatment admission, and the appropriate services can then be targeted to that patient as part of the overall treatment. It's not very different from what most treatment clinicians describe as individually tailored treatment."

Source

- McLellan, A.T.; Grissom, G.R.; Zanis, D.; Randall, M.; Brill, P.; O'Brien, C.P. Problem-service "matching" in addiction treatment: A prospective study in 4 programs. *Archives of General Psychiatry* 54:730-735, 1997. 

NIDA Manual Shows Managers How to Analyze Their Substance Abuse Treatment Programs

By Steven Stocker, *NIDA NOTES* Contributing Writer

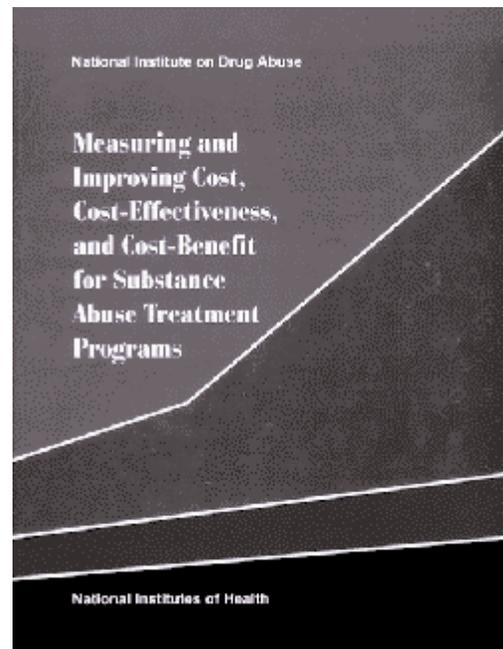
A new NIDA resource provides substance abuse treatment program managers with tools to calculate the costs of their programs and to investigate the relationship between these costs and various treatment outcomes. These analyses can help program managers reduce costs and improve treatment while demonstrating to funders that the programs deserve support.

"In recent years, competition for substance abuse program funds has become more intense," says NIDA Director Dr. Alan I. Leshner. "At the same time, program costs and the relationship between these costs and outcomes have come under greater scrutiny. Program managers need to learn how to analyze their programs so that they can provide concrete evidence that the programs are a good investment of public and private funds."

The new manual, *Measuring and Improving Cost, Cost-Effectiveness, and Cost-Benefit for Substance Abuse Treatment Programs*, was written for NIDA by Dr. Brian Yates of American University in Washington, D.C. The manual is designed to guide professionals from diverse disciplines and educational backgrounds through the collection and analysis of data on program costs, treatment procedures, patient processes, and program outcomes. The manual provides step-by-step instructions, exercises, and worksheets and explains how to analyze data using graphs and spreadsheets. Numerous examples from real-life situations illustrate how the analyses can be used in different programs.

In the section on cost analysis, the manual describes methods for collecting data on the costs of treatment personnel, space, equipment, and other expenses, including donated resources, such as volunteer services or equipment. By incorporating all resources—both paid and donated—into the analysis, program managers can help other service providers attempting to replicate the program see what costs will be if they cannot obtain the same level of donated resources.

The manual also describes how to measure patient outcomes. Outcome measures may be nonmonetary, such as the number of days drug-free or number of days employed. Measures may also be monetary, such as cost savings resulting from reduced use of criminal justice, social, and health services as an outcome of substance abuse treatment.



The data on costs and patient outcomes can be used together to produce cost-effectiveness and cost-benefit analyses. Cost-effectiveness analyses show the relationship between a program's costs and nonmonetary patient outcomes. These analyses can be used to compare one program to another or to compare different components of the same program. A program or component is considered more cost-effective than another when it either produces the same outcome at a lower cost or produces a better outcome at the same cost.

Cost-benefit analyses show the relationship between a program's costs and monetary patient outcomes. Like cost-effectiveness analysis, cost-benefit analysis can be used to compare one program to another or to compare different components within the same program. Cost-benefit analyses can be used noncomparatively as well. For example, a cost-benefit analysis may find that every \$1 spent on a particular substance abuse treatment program results in an average savings of \$5 to taxpayers due to reductions in criminal justice and medical costs.

Program managers can use cost-effectiveness and cost-benefit analyses to evaluate their programs to determine how

to enhance outcomes and reduce costs. These analyses can also give funding sources and policymakers concrete evidence of a program's effectiveness.

"Analyzing the costs, cost-effectiveness, and cost-benefits of substance abuse treatment programs is sometimes complex because there are so many variables to consider," says Dr. Peter Delany of NIDA's Services Research Branch. "This manual, which was field-tested by program managers, provides clear and concise explanations of these analyses for managers who are interested in evaluating their programs."

To Receive This Resource

Free copies of Measuring and Improving Cost, Cost-Effectiveness, and Cost-Benefit for Substance Abuse Treatment Programs are available from the National Clearinghouse for Alcohol and Drug Information (NCADI), P.O. Box 2345, Rockville, MD 20847-2345; (800) 729-6686 or (301) 468-2600; TDD number: (800) 487-4889; fax: (301) 468-6433; e-mail: info@health.org. The manual is also available in the Health Services Research section of NIDA's home page at www.drugabuse.gov. 

New Report Provides Information On Cocaine Abuse and Treatment

To help inform the public about the harmful effects of cocaine abuse and aid in prevention and treatment efforts, NIDA has issued a new Research Report, "Cocaine Abuse and Addiction." The 8-page report summarizes the latest scientific findings about the nature and extent of cocaine abuse and addiction, the consequences of cocaine abuse, and effective treatments for those addicted to cocaine.

The report is the latest in a series of NIDA *Research Reports* on abused drugs. Other Research Reports cover methamphetamine, nicotine, heroin, inhalants, and anabolic steroids. Highlights from "Cocaine Abuse and Addiction" are below.



What is cocaine?

Cocaine is a powerfully addictive drug that directly affects the brain. The drug has two basic chemical forms: a powdered form and a nonpowdered form. The powdered form can be taken orally or intranasally, rubbed onto mucous tissues, or dissolved in water and injected intravenously. The nonpowdered form, which is processed from the powdered form, is called "crack" on the street and can be smoked.

How does cocaine produce its effects?

Cocaine blocks reabsorption of a neurotransmitter called dopamine by nerve cells, or neurons, in one of the brain's key pleasure centers. The resulting buildup of dopamine in the space between nerve cells causes continuous stimulation of receiving neurons. Scientists believe this action plays a major role in the euphoria reported by cocaine abusers.

What are the short-term effects of cocaine use?

Cocaine's effects appear almost immediately and disappear in a few minutes or hours, depending on the route of administration. Injected and smoked cocaine produces intense effects rapidly. Small amounts make the user feel euphoric, energetic, talkative, and alert. Large amounts intensify these feelings but may lead to bizarre, erratic, and violent behavior. Physiological effects include constricted blood vessels, dilated pupils, and increased temperature, heart rate, and blood pressure. Some users report feelings of restlessness, irritability, and anxiety. In rare instances, sudden death can occur, usually from cardiac arrest followed by respiratory arrest.

What are the long-term effects of cocaine use?

Addiction, irritability, mood disturbances, restlessness, paranoia, and auditory hallucinations are among the possible long-term consequences of repeated cocaine use.

What are the medical consequences of cocaine abuse?

Cardiovascular effects include disturbances in heart rhythm and heart attacks. Respiratory effects include chest pain and respiratory failure. Strokes, seizures, and headaches are among the neurological effects. Gastrointestinal complications include abdominal pain and nausea. Cocaine abusers, especially those who inject the drug, also are at increased risk of infectious diseases, such as HIV/AIDS and hepatitis.

What treatments are effective for cocaine abuse?

Many behavioral treatments have been found to be effective in treating cocaine addiction when they are matched to the needs of the individual patient. Contingency management, cognitive-behavioral coping skills treatment, and therapeutic communities all have been effective with cocaine-addicted patients. Contingency management rewards patients for staying in treatment and remaining cocaine-free. Short-term cognitive-behavioral coping skills treatment helps patients recognize and avoid situations in which they are likely to use cocaine and learn to cope more effectively with their problems. Therapeutic communities are long-term residential programs that offer a full range of rehabilitative and support services for cocaine-addicted patients with severe problems. No medications

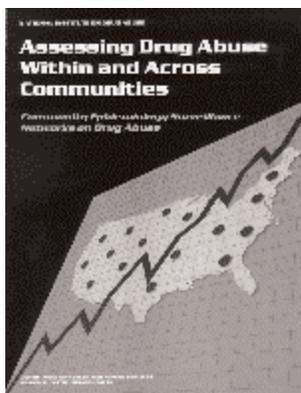
are currently available to treat cocaine addiction. However, several promising treatment compounds are being tested for safety and efficacy.

For More Information

The NIDA *Research Report* "Cocaine Abuse and Addiction" (NCADI publication #PHD813) can be obtained from the National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD 20847, 1-800-729-6686. All reports in the NIDA Research Report series and additional information about cocaine can be found on the NIDA home page on the World Wide Web at www.nida.nih.gov. 

New Drug Abuse Prevention and Treatment Resources for Communities and Treatment Providers

Three new NIDA publications offer research-based information on preventing and treating drug abuse for communities, drug abuse treatment providers, and others. The publications continue NIDA's campaign to disseminate current research information and expedite its use. All three publications are free of charge.



Assessing Drug Abuse Within and Across Communities: Community Epidemiology Surveillance Networks on Drug Abuse

(NIH Publication Number 98-3614)

Research has shown that to succeed, drug abuse prevention and treatment programs must be tailored to specific community needs. This new

guidebook is designed to help communities, cities, counties, and States determine the extent of drug abuse problems in their areas and develop the most effective prevention and treatment programs for their needs. The 124-page volume explains why community epidemiology surveillance networks are necessary and how communities can create their own networks to identify local drug use patterns and trends. The guidebook also tells how to obtain drug use data and contains sample forms and other tools to help with data collection and organization. *Assessing Drug Abuse* is based on the experience of NIDA's Community Epidemiology Work Group, a network of researchers that has monitored national drug abuse trends in the United States for more than 20 years.

Therapy Manuals for Drug Addiction Series

NIDA has released the first two manuals in this series, which is being developed to help treatment providers and mental health professionals obtain and use up-to-date research information on effective approaches to treating drug addiction.

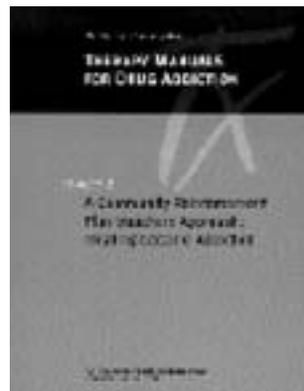


Manual One. A Cognitive-Behavioral Approach: Treating Cocaine Addiction

(NIH Publication Number 98-4308)

This 127-page manual describes a cognitive behavioral therapy (CBT) program developed by researchers at Yale University in New Haven, Connecticut, for treating addiction. CBT is a

short-term, flexible approach and is clinically proven to help individuals recognize and avoid situations in which they may use drugs. The program teaches drug abusers in treatment to use coping skills to solve problems linked with drug use, such as difficult family relationships or losing a job. The manual provides an overview of the basic principles of CBT and explains the structure and topics to be used in treatment sessions.



Manual Two. A Community Reinforcement Plus Vouchers Approach: Treating Cocaine Addiction

(NIH Publication Number 98-4309)

This manual guides drug abuse treatment providers in using a community reinforcement plus vouchers approach, a behavioral strategy for treating cocaine addiction that has

been proven effective in clinical trials. This multicomponent treatment approach combines community reinforcement, including individual counseling and skills training, with an incentive program using vouchers. Therapists tailor the individual counseling and skills training sessions to each patient's needs. As long as the patient remains in treatment and abstinent from cocaine, he or she earns points that can be exchanged for vouchers to receive

incentives, such as fishing licenses or gift certificates to restaurants or shops. The 148-page manual gives step-by-step instructions for implementing the community reinforcement plus vouchers approach, including the style, technique, and structure of counseling needed. The manual also describes the format to be used for initial counseling sessions and training sessions on drug avoidance skills.

Free copies of these three publications are available by contacting the National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD 20847-2345; (800) 729-6686 or (301) 468-2600; TDD number: (800) 487-4889; fax: (301) 468-6433; e-mail: info@health.org. **NI**